

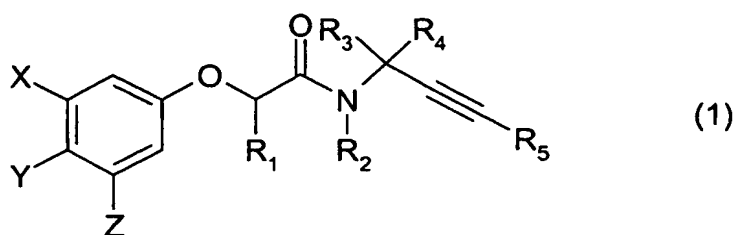
# FUNGICIDES

This invention relates to novel *N*-alkynyl-2-(substituted phenoxy)alkylamides, to processes for preparing them, to compositions containing them and to methods of using them to combat fungi, especially fungal infections of plants.

Certain *N*-alkynyl-2-(substituted phenoxy)alkylamides are described in US 4,116,677 and US 4,070,486 as being useful as herbicides or miticides. Others are described in US 4,168,319 as being useful as mildewicides.

The present invention is concerned with the provision of particular *N*-alkynyl-2-(substituted phenoxy)alkylamides for use as plant fungicides.

Thus according to the present invention there is provided a compound of the general formula (1):



wherein

X, Y and Z are independently H, halogen, C<sub>1-4</sub> alkyl (e.g. methyl), halo(C<sub>1-4</sub>)alkyl (e.g. trifluoromethyl), C<sub>2-4</sub> alkenyl, halo(C<sub>2-4</sub>)alkenyl, C<sub>2-4</sub> alkynyl, halo(C<sub>2-4</sub>)alkynyl, C<sub>1-4</sub> alkoxy (e.g. methoxy), halo(C<sub>1-4</sub>)alkoxy (e.g. trifluoromethoxy), -S(O)<sub>n</sub>(C<sub>1-4</sub>)alkyl where n is 0, 1 or 2 and the alkyl group is optionally substituted with fluoro (e.g. methylthio, trifluoromethylsulphonyl), -OSO<sub>2</sub>(C<sub>1-4</sub>)alkyl where the alkyl group is optionally substituted with fluoro (e.g. trifluoromethylsulphonyloxy), cyano, nitro, C<sub>1-4</sub> alkoxy-carbonyl, -CONR'R'', -COR', -NR'COR'' or -NR'COOR''' where R' and R'' are independently H or C<sub>1-4</sub> alkyl and R''' is C<sub>1-4</sub> alkyl (e.g. acetyl, -NHCOCH<sub>3</sub> and -NHCO<sub>2</sub>CH<sub>3</sub>), provided that at least one of X and Z is other than H;

R<sub>1</sub> is C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl or C<sub>2-4</sub> alkynyl in which the alkyl, alkenyl and alkynyl groups are optionally substituted on their terminal carbon atom with one, two or three halogen atoms (e.g. 2,2,2-trifluoroethyl), with a cyano group (e.g. cyanomethyl), with a C<sub>1-4</sub> alkyl-carbonyl group (e.g. acetylmethyl), with a C<sub>1-4</sub> alkoxy-carbonyl group (e.g. methoxycarbonylmethyl and methoxycarbonylethyl) or with a hydroxy group (e.g.

hydroxymethyl);

R<sub>2</sub> is H, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxymethyl or benzyloxymethyl in which the phenyl ring of the benzyl moiety is optionally substituted with C<sub>1-4</sub> alkoxy;

5 R<sub>3</sub> and R<sub>4</sub> are independently H, C<sub>1-3</sub> alkyl, C<sub>2-3</sub> alkenyl or C<sub>2-3</sub> alkynyl provided that both are not H and that when both are other than H their combined total of carbon atoms does not exceed 4, or

R<sub>3</sub> and R<sub>4</sub> join with the carbon atom to which they are attached to form a 3 or 4 membered carbocyclic ring optionally containing one O, S or N atom and optionally substituted with halo or C<sub>1-4</sub> alkyl; and

10 R<sub>5</sub> is unsubstituted C<sub>3-4</sub> alkyl, unsubstituted C<sub>3-6</sub> cycloalkyl or C<sub>1-4</sub> alkyl or C<sub>3-6</sub> cycloalkyl in which the alkyl and cycloalkyl groups are substituted with halo, hydroxy, C<sub>1-6</sub> alkoxy, cyano, C<sub>1-4</sub> alkylcarbonyloxy, aminocarbonyloxy, mono- or di(C<sub>1-4</sub>)alkylaminocarbonyloxy, -S(O)<sub>n</sub>(C<sub>1-6</sub>)alkyl where n is 0, 1 or 2, triazolyl (e.g. 1,2,4-triazol-1-yl), tri(C<sub>1-4</sub>)alkylsilyloxy, optionally substituted phenoxy, optionally substituted  
15 thienyloxy, optionally substituted benzyloxy or optionally substituted thienylmethoxy, in which the optionally substituted phenyl and thienyl rings of phenoxy, thienyloxy, benzyloxy and thienylmethoxy are optionally substituted with one, two or three substituents selected from halo, hydroxy, mercapto, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> alkoxy, C<sub>2-4</sub> alkenyloxy, C<sub>2-4</sub> alkynyloxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, C<sub>1-4</sub>  
20 alkylthio, halo(C<sub>1-4</sub>)alkylthio, hydroxy(C<sub>1-4</sub>)alkyl, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR<sup>m</sup>R<sup>n</sup>, -NHCOR<sup>m</sup>, -NHCONR<sup>m</sup>R<sup>n</sup>, -CONR<sup>m</sup>R<sup>n</sup>, -SO<sub>2</sub>R<sup>m</sup>, -OSO<sub>2</sub>R<sup>m</sup>, -COR<sup>m</sup>, -CR<sup>m</sup>=NR<sup>n</sup> or -N=CR<sup>m</sup>R<sup>n</sup>, in which R<sup>m</sup> and R<sup>n</sup> are  
25 alkylthio, C<sub>3-6</sub> cycloalkyl, C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy.

The compounds of the invention contain at least one asymmetric carbon atom (and at least two when R<sub>3</sub> and R<sub>4</sub> are different) and may exist as enantiomers (or as pairs of diastereoisomers) or as mixtures of such. However, these mixtures may be separated  
30 into individual isomers or isomer pairs, and this invention embraces such isomers and mixtures thereof in all proportions. It is to be expected that for any given compound, one isomer may be more fungicidally active than another.

Except where otherwise stated, alkyl groups and alkyl moieties of alkoxy, alkylthio, etc., suitably contain from 1 to 4 carbon atoms in the form of straight or branched chains. Examples are methyl, ethyl, *n*- and *iso*-propyl and *n*-, *sec*-, *iso*- and *tert*-butyl. Where alkyl moieties contain 5 or 6 carbon atoms, examples are *n*-pentyl and *n*-hexyl.

Alkenyl and alkynyl moieties also suitable contain from 2 to 4 carbon atoms in the form of straight or branched chains. Examples are allyl, ethynyl and propargyl.

Halo includes fluoro, chloro, bromo and iodo. Most commonly it is fluoro, chloro or bromo and usually fluoro or chloro.

The substituents X, Y and Z on the phenyl ring of formula (1) may provide a 3-, 3, 5- or 3, 4, 5- substituted phenyl ring. Typically X, Y and Z are all chloro or methyl, or X and Z are both chloro or bromo and Y is H or methyl, or X and Z are both methyl or methoxy and Y is H, chloro, bromo or alkylthio, or X is methoxy, Y is H and Z is cyano or chloro, or X is methyl, Y is H and Z is ethyl, or X is chloro, bromo or trifluoromethyl and both Y and Z are H.

Typically, R<sub>1</sub> is methyl, ethyl, *n*-propyl, 2,2,2-trifluoromethyl, cyanomethyl, acetylmethyl, methoxycarbonylmethyl, methoxycarbonylethyl, hydroxymethyl, hydroxyethyl. Ethyl is a preferred value of R<sub>1</sub>.

Typically R<sub>2</sub> is H and at least one, but preferably both of R<sub>3</sub> and R<sub>4</sub> are methyl. When one of R<sub>3</sub> and R<sub>4</sub> is H, the other may be methyl, ethyl or *n*- or *iso*-propyl. When one of R<sub>3</sub> and R<sub>4</sub> is methyl, the other may be H or ethyl but is preferably also methyl. R<sub>2</sub> also includes C<sub>1-4</sub> alkoxymethyl and benzyloxymethyl in which the phenyl ring of the benzyl group optionally carries an alkoxy substituent, e.g. a methoxy substituent. Such values of R<sub>2</sub> provide compounds of formula (1) that are believed to be pro-pesticidal compounds.

Typically R<sub>5</sub> is *n*-propyl, hydroxymethyl, methoxymethyl, 1-methoxyethyl, *tert*-butyldimethylsilyloxymethyl, 3-chloropropyl, 3-cyanopropyl, 3-methoxypropyl, 3-(1,2,4-triazol-1-yl)propyl, 3-methylthiopropyl, 3-methanesulphinylpropyl or 3-methanesulphonylpropyl. Of particular interest are compounds where R<sub>5</sub> is hydroxymethyl, methoxymethyl, 1-methoxyethyl or *tert*-butyldimethylsilyloxymethyl. Also of particular interest are compounds where R<sub>5</sub> is 3-cyanopropyl, 3-methoxypropyl, 3-(1,2,4-triazol-1-yl)propyl, 3-methylthiopropyl, 3-methanesulphinylpropyl or 3-methanesulphonylpropyl.

In one aspect the invention provides a compound of the general formula (1) wherein

- X, Y and Z are independently H, halogen, C<sub>1-4</sub> alkyl (e.g. methyl), halo(C<sub>1-4</sub>)alkyl (e.g. trifluoromethyl), C<sub>2-4</sub> alkenyl, halo(C<sub>2-4</sub>)alkenyl, C<sub>2-4</sub> alkynyl, halo(C<sub>2-4</sub>)alkynyl, C<sub>1-4</sub> alkoxy (e.g. methoxy), halo(C<sub>1-4</sub>)alkoxy (e.g. trifluoromethoxy), -S(O)<sub>n</sub>(C<sub>1-4</sub>)alkyl where n is 0, 1 or 2 and the alkyl group is optionally substituted with fluoro (e.g. methylthio, trifluoromethylsulphonyl), -OSO<sub>2</sub>(C<sub>1-4</sub>)alkyl where the alkyl group is optionally substituted with fluoro (e.g. trifluoromethylsulphonyloxy), cyano, nitro, C<sub>1-4</sub> alkoxycarbonyl, -CONR'R", -COR' or -NR'COR" where R' and R" are independently H or C<sub>1-4</sub> alkyl (e.g. -NHCOCH<sub>3</sub>), provided that at least one of X and Z is other than H;
- R<sub>1</sub> is C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl or C<sub>2-4</sub> alkynyl in which the alkyl, alkenyl and alkynyl groups are optionally substituted on their terminal carbon atom with one, two or three halogen atoms (e.g. 2,2,2-trifluoroethyl), with a cyano group (e.g. cyanomethyl), with a C<sub>1-4</sub> alkylcarbonyl group (e.g. acetylmethyl), with a C<sub>1-4</sub> alkoxycarbonyl group (e.g. methoxycarbonylmethyl and methoxycarbonylethyl) or with a hydroxy group (e.g. hydroxymethyl);
- R<sub>2</sub> is H, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxymethyl or benzyloxymethyl in which the phenyl ring of the benzyl moiety is optionally substituted with C<sub>1-4</sub> alkoxy;
- R<sub>3</sub> and R<sub>4</sub> are independently H, C<sub>1-3</sub> alkyl, C<sub>2-3</sub> alkenyl or C<sub>2-3</sub> alkynyl provided that both are not H and that when both are other than H their combined total of carbon atoms does not exceed 4, or R<sub>3</sub> and R<sub>4</sub> join with the carbon atom to which they are attached to form a 3 or 4 membered carbocyclic ring optionally containing one O, S or N atom and optionally substituted with halo or C<sub>1-4</sub> alkyl; and
- R<sub>5</sub> is C<sub>1-4</sub> alkyl or C<sub>3-6</sub> cycloalkyl in which the alkyl and cycloalkyl groups are substituted with hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkylthio, tri(C<sub>1-4</sub>)alkylsilyloxy, optionally substituted phenoxy, optionally substituted thienyloxy, optionally substituted benzyloxy or optionally substituted thienylmethoxy, in which the optionally substituted phenyl and thienyl rings of phenoxy, thienyloxy, benzyloxy and thienylmethoxy are optionally substituted with one, two or three substituents selected from halo, hydroxy, mercapto, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> alkoxy, C<sub>2-4</sub> alkenyloxy, C<sub>2-4</sub> alkynyloxy, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, C<sub>1-4</sub> alkylthio, halo(C<sub>1-4</sub>)alkylthio, hydroxy(C<sub>1-4</sub>)alkyl, C<sub>1-4</sub>alkoxy(C<sub>1-4</sub>)alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl, phenoxy, benzyloxy, benzoyloxy, cyano, isocyano, thiocyanato, isothiocyanato, nitro, -NR<sup>m</sup>R<sup>n</sup>, -NHCOR<sup>m</sup>, -NHCONR<sup>m</sup>R<sup>n</sup>,

-CONR<sup>m</sup>R<sup>n</sup>, --SO<sub>2</sub>R<sup>m</sup>, -OSO<sub>2</sub>R<sup>m</sup>, -COR<sup>m</sup>, -CR<sup>m</sup>=NR<sup>n</sup> or -N=CR<sup>m</sup>R<sup>n</sup>, in which R<sup>m</sup> and R<sup>n</sup> are independently hydrogen, C<sub>1-4</sub> alkyl, halo(C<sub>1-4</sub>)alkyl, C<sub>1-4</sub> alkoxy, halo(C<sub>1-4</sub>)alkoxy, C<sub>1-4</sub> alkylthio, C<sub>3-6</sub> cycloalkyl, C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl, phenyl or benzyl, the phenyl and benzyl groups being optionally substituted with halogen, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy.

- 5 In another aspect, the invention provides a compound of the general formula (1) wherein X, Y and Z are all chloro or methyl, or X and Z are both chloro or bromo and Y is H or methyl, or X and Z are both methyl or methoxy and Y is H, chloro, bromo or alkylthio, or X is methoxy, Y is H and Z is cyano or chloro, or X is methyl, Y is H and Z is ethyl, or X is chloro, bromo or trifluoromethyl and both Y and Z are H; R<sub>1</sub> is methyl,  
 10 ethyl, *n*-propyl, 2,2,2-trifluoromethyl, cyanomethyl, acetylmethyl, methoxycarbonylmethyl, methoxycarbonyl-ethyl, hydroxymethyl or hydroxyethyl; R<sub>2</sub> is H; R<sub>3</sub> and R<sub>4</sub> are both methyl; and R<sub>5</sub> is hydroxymethyl, methoxymethyl, 1-methoxyethyl, *tert*-butyldimethylsiloxymethyl, 3-chloropropyl, 3-cyanopropyl, 3-methoxypropyl, 3-(1,2,4-triazol-1-yl)propyl, 3-methylthiopropyl, 3-methanesulphinylpropyl or 3-methanesulphonyl-  
 15 propyl. Preferably R<sub>1</sub> is ethyl. Preferably R<sub>5</sub> is methoxymethyl or 3-cyanopropyl.

Compounds that form part of the invention are illustrated in Tables 1 to 57 below.

The compounds in Table 1 are of the general formula (1) where R<sub>1</sub> is ethyl, R<sub>2</sub> is H, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is hydroxymethyl and X, Y and Z have the values given in the table.

20 Table 1

Compound No	X	Y	Z
1	Cl	Cl	CN
2	Cl	Cl	Cl
3	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>
4	Cl	H	Cl
5	Cl	CH <sub>3</sub>	Cl
6	Br	H	Br
7	Br	CH <sub>3</sub>	Br
8	CH <sub>3</sub>	H	CH <sub>3</sub>
9	CH <sub>3</sub>	Cl	CH <sub>3</sub>
10	CH <sub>3</sub>	Br	CH <sub>3</sub>
11	CH <sub>3</sub>	CH <sub>3</sub> S	CH <sub>3</sub>

12	CH <sub>3</sub> O	H	CH <sub>3</sub> O
13	CH <sub>3</sub> O	Cl	CH <sub>3</sub> O
14	CH <sub>3</sub> O	Br	CH <sub>3</sub> O
15	CH <sub>3</sub> O	CH <sub>3</sub> S	CH <sub>3</sub> O
16	CH <sub>3</sub> O	H	CN
17	CH <sub>3</sub> O	H	Cl
18	CH <sub>3</sub>	H	C <sub>2</sub> H <sub>5</sub>
19	Cl	H	H
20	Br	H	H
21	CF <sub>3</sub>	H	H
22	Br	Cl	H
23	Br	Br	H
24	Br	F	H
25	Br	CN	H
26	Br	CF <sub>3</sub> O	H
27	Br	CH <sub>3</sub> S	H
28	Br	HC≡C-	H
29	Br	CH <sub>2</sub> =CH-	H
30	Br	CH <sub>3</sub> O	H
31	Br	COCH <sub>3</sub>	H
32	Br	CF <sub>3</sub>	H
33	F	H	H
34	CN	H	H
35	CH <sub>3</sub>	H	H
36	CH <sub>3</sub> CO	H	H
37	CH <sub>3</sub> O	H	H
38	CF <sub>3</sub> O	H	H
39	CH <sub>3</sub> S	H	H
40	HC≡C-	H	H
41	H <sub>2</sub> C=CH-	H	H
42	F	H	F
43	F	H	Cl

44	F	H	Br
45	F	H	CH <sub>3</sub> O
46	F	H	CH <sub>3</sub> CO
47	F	H	CN
48	F	H	CH <sub>3</sub>
49	F	H	CF <sub>3</sub> O
50	F	H	CF <sub>3</sub>
51	F	H	CH <sub>3</sub> S
52	F	H	COOCH <sub>3</sub>
53	Cl	H	Br
54	Cl	H	CH <sub>3</sub> CO
55	Cl	H	CH <sub>3</sub>
56	Cl	H	CN
57	Cl	H	CF <sub>3</sub> O
58	Cl	H	CF <sub>3</sub>
59	Cl	H	CH <sub>3</sub> S
60	Cl	H	COOCH <sub>3</sub>
61	Cl	H	CON(CH <sub>3</sub> ) <sub>2</sub>
62	Cl	H	NHCOOCH <sub>3</sub>
63	Cl	H	OSO <sub>2</sub> CH <sub>3</sub>
64	Cl	H	HC≡C-
65	Cl	H	CH <sub>2</sub> =CH-
66	Br	H	CH <sub>3</sub>
67	Br	H	CN
68	CN	H	CN
69	CN	H	CH <sub>3</sub>
70	CN	H	CF <sub>3</sub> O
71	CF <sub>3</sub> O	H	CF <sub>3</sub> O
72	CF <sub>3</sub>	H	CF <sub>3</sub>
73	CH <sub>3</sub>	H	CH <sub>3</sub> O
74	F	F	H
75	F	Cl	H

76	F	Br	H
77	F	CH <sub>3</sub> O	H
78	F	CN	H
79	F	CH <sub>3</sub>	H
80	Cl	Cl	H
81	Cl	F	H
82	Cl	Br	H
83	Cl	CN	H
84	Cl	CH <sub>3</sub>	H
85	Cl	CH <sub>3</sub> O	H
86	Cl	CF <sub>3</sub> O	H
87	Cl	CH <sub>3</sub> S	H
88	Cl	CH <sub>3</sub> SO <sub>2</sub> O	H
89	Cl	CH <sub>3</sub> CO	H
90	CN	F	H
91	CN	Cl	H
92	CN	CH <sub>3</sub> O	H
93	CH <sub>3</sub> O	CH <sub>3</sub> O	H
94	CH <sub>3</sub> O	Cl	H
95	CH <sub>3</sub> O	CN	H
96	CH <sub>3</sub> CO	Cl	H
97	CF <sub>3</sub> O	Cl	H
98	CF <sub>3</sub> O	CN	H
99	CH <sub>3</sub> S	Cl	H
100	CH <sub>3</sub> S	F	H
101	CH <sub>3</sub> S	CH <sub>3</sub>	H
102	CH <sub>3</sub> SO <sub>2</sub> O	Cl	H
103	Cl	Cl	F
104	Cl	Cl	Br
105	Cl	Cl	CH <sub>3</sub> O
106	Cl	Cl	CH <sub>3</sub> CO
107	Cl	Cl	CH <sub>3</sub> S



108	Cl	F	Cl
109	Cl	CH <sub>3</sub> O	Cl
110	Cl	CF <sub>3</sub> O	Cl
111	Cl	CH <sub>3</sub> SO	Cl
112	Cl	CH <sub>3</sub> SO <sub>2</sub>	Cl
113	Cl	OSO <sub>2</sub> CH <sub>3</sub>	Cl
114	Cl	CH <sub>3</sub> CO	Cl
115	Cl	CO <sub>2</sub> CH <sub>3</sub>	Cl
116	Cl	CON(CH <sub>3</sub> ) <sub>2</sub>	Cl
117	Cl	HC≡C-	Cl
118	Cl	CH <sub>2</sub> =CH-	Cl
119	Cl	NHCO <sub>2</sub> CH <sub>3</sub>	Cl
120	F	F	F
121	F	F	CN
122	F	F	CH <sub>3</sub>
123	F	F	CH <sub>3</sub> O
124	F	CH <sub>3</sub> O	F
125	F	CF <sub>3</sub> O	F
126	F	CH <sub>3</sub> SO	F
127	F	CH <sub>3</sub> SO <sub>2</sub>	F
128	F	OSO <sub>2</sub> CH <sub>3</sub>	F
129	F	CH <sub>3</sub> CO	F
130	F	CO <sub>2</sub> CH <sub>3</sub>	F
131	CH <sub>3</sub> O	CH <sub>3</sub> O	CH <sub>3</sub> O
132	CH <sub>3</sub> O	CH <sub>3</sub> O	Cl
133	CH <sub>3</sub> O	CH <sub>3</sub> O	CH <sub>3</sub>
134	Cl	CN	Cl

Table 2

Table 2 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methyl, R<sub>2</sub> is  
5 hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is hydroxymethyl and X, Y and Z have the

values listed in Table 1. Thus compound 1 of Table 2 is the same as compound 1 of Table 1 except that in compound 1 of Table 2  $R_1$  is methyl instead of ethyl. Similarly, compounds 2 to 134 of Table 2 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 2  $R_1$  is methyl instead of ethyl.

5 Table 3

Table 3 consists of 134 compounds of the general formula (1), where  $R_1$  is *n*-propyl,  $R_2$  is hydrogen,  $R_3$  and  $R_4$  are both methyl, and  $R_5$  is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 3 is the same as compound 1 of Table 1 except that in compound 1 of Table 3  $R_1$  is *n*-propyl instead of ethyl. Similarly, compounds 2 to 134 of Table 3 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 3  $R_1$  is *n*-propyl instead of ethyl.

Table 4

Table 4 consists of 134 compounds of the general formula (1), where  $R_1$  is 2,2,2-trifluoromethyl,  $R_2$  is hydrogen,  $R_3$  and  $R_4$  are both methyl,  $R_5$  is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 4 is the same as compound 1 of Table 1 except that in compound 1 of Table 4  $R_1$  is 2,2,2-trifluoromethyl instead of ethyl. Similarly, compounds 2 to 134 of Table 4 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 4  $R_1$  is 2,2,2-trifluoromethyl instead of ethyl.

20 Table 5

Table 5 consists of 134 compounds of the general formula (1), where  $R_1$  is cyanomethyl,  $R_2$  is hydrogen,  $R_3$  and  $R_4$  are both methyl,  $R_5$  is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 5 is the same as compound 1 of Table 1 except that in compound 1 of Table 5  $R_1$  is cyanomethyl instead of ethyl. Similarly, compounds 2 to 134 of Table 5 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 4  $R_1$  is cyanomethyl instead of ethyl.

Table 6

Table 6 consists of 134 compounds of the general formula (1), where  $R_1$  is acetylmethyl,  $R_2$  is hydrogen,  $R_3$  and  $R_4$  are both methyl,  $R_5$  is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 6 is the same as compound 1 of Table 1 except that in compound 1 of Table 6  $R_1$  is acetylmethyl instead of ethyl. Similarly, compounds 2 to 134 of Table 6 are the same as compounds 2 to 134 of Table

1, respectively, except that in the compounds of Table 4 R<sub>1</sub> is acetylmethyl instead of ethyl.

#### Table 7

Table 7 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 7 is the same as compound 1 of Table 1 except that in compound 1 of Table 7 R<sub>1</sub> is methoxycarbonylmethyl instead of ethyl. Similarly, compounds 2 to 134 of Table 7 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 7 R<sub>1</sub> is methoxycarbonylmethyl instead of ethyl.

#### Table 8

Table 8 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 8 is the same as compound 1 of Table 1 except that in compound 1 of Table 8 R<sub>1</sub> is methoxycarbonylethyl instead of ethyl. Similarly, compounds 2 to 134 of Table 8 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 8 R<sub>1</sub> is methoxycarbonylethyl instead of ethyl.

#### Table 9

Table 9 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxymethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 9 is the same as compound 1 of Table 1 except that in compound 1 of Table 9 R<sub>1</sub> is hydroxymethyl instead of ethyl. Similarly, compounds 2 to 134 of Table 9 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 9 R<sub>1</sub> is hydroxymethyl instead of ethyl.

#### Table 10

Table 10 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxyethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is hydroxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 10 is the same as compound 1 of Table 1 except that in compound 1 of Table 10 R<sub>1</sub> is hydroxyethyl instead of ethyl. Similarly, compounds 2 to 134 of Table 10 are the same as compounds 2 to 134

of Table 1, respectively, except that in the compounds of Table 10 R<sub>1</sub> is hydroxyethyl instead of ethyl.

#### Table 11

Table 11 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 11 is the same as compound 1 of Table 1 except that in compound 1 of Table 11 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 11 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 11 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 12

Table 12 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1 for compounds 1 to 134. Thus compound 1 of Table 12 is the same as compound 1 of Table 2 except that in compound 1 of Table 12 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 12 are the same as compounds 2 to 134 of Table 2, respectively, except that in the compounds of Table 12 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 13

Table 13 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is *n*-propyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, and R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 13 is the same as compound 1 of Table 3 except that in compound 1 of Table 13 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 13 are the same as compounds 2 to 134 of Table 3, respectively, except that in the compounds of Table 13 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 14

Table 14 consists of 134 compounds of the general formula (1), where R<sub>1</sub> 2,2,2-trifluoromethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 14 is the same as compound 1 of Table 4 except that in compound 1 of Table 14 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 14 are the same as compounds 2

to 134 of Table 4, respectively, except that in the compounds of Table 14 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 15

Table 15 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is cyanomethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 15 is the same as compound 1 of Table 5 except that in compound 1 of Table 15 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 15 are the same as compounds 2 to 134 of Table 5, respectively, except that in the compounds of Table 15 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 16

Table 16 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is acetylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 16 is the same as compound 1 of Table 6 except that in compound 1 of Table 16 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 16 are the same as compounds 2 to 134 of Table 6, respectively, except that in the compounds of Table 16 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 17

Table 17 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 17 is the same as compound 1 of Table 7 except that in compound 1 of Table 17 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 17 are the same as compounds 2 to 134 of Table 7, respectively, except that in the compounds of Table 17 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 18

Table 18 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 18 is the same as compound 1 of Table 8 except that in compound 1 of Table 18 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 18 are the

same as compounds 2 to 134 of Table 8, respectively, except that in the compounds of Table 18 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 19

Table 19 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxymethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 19 is the same as compound 1 of Table 9 except that in compound 1 of Table 19 R<sub>5</sub> is methoxymethyl instead of methyl. Similarly, compounds 2 to 134 of Table 19 are the same as compounds 2 to 134 of Table 9, respectively, except that in the compounds of Table 19 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 20

Table 20 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxyethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is methoxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 20 is the same as compound 1 of Table 10 except that in compound 1 of Table 20 R<sub>5</sub> is methoxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 20 are the same as compounds 2 to 134 of Table 10, respectively, except that in the compounds of Table 20 R<sub>1</sub> is methoxymethyl instead of hydroxymethyl.

#### Table 21

Table 21 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 21 is the same as compound 1 of Table 1 except that in compound 1 of Table 21 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 21 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 21 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 22

Table 22 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1 for compounds 1 to 134. Thus compound 1 of Table 22 is the same as compound 1 of Table 2 except that in compound 1 of Table 22 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 22 are the same as compounds 2 to 134 of Table 2, respectively, except that

in the compounds of Table 22 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 23

Table 23 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is *n*-propyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, and R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 23 is the same as compound 1 of Table 3 except that in compound 1 of Table 23 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 23 are the same as compounds 2 to 134 of Table 3, respectively, except that in the compounds of Table 23 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 24

Table 24 consists of 134 compounds of the general formula (1), where R<sub>1</sub> 2,2,2-trifluoromethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 24 is the same as compound 1 of Table 4 except that in compound 1 of Table 24 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 24 are the same as compounds 2 to 134 of Table 4, respectively, except that in the compounds of Table 24 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 25

Table 25 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is cyanomethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 25 is the same as compound 1 of Table 5 except that in compound 1 of Table 25 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 25 are the same as compounds 2 to 134 of Table 5, respectively, except that in the compounds of Table 25 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 26

Table 26 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is acetylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 26 is the same as compound 1 of Table 6 except that in compound 1 of Table 26 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 26 are

the same as compounds 2 to 134 of Table 6, respectively, except that in the compounds of Table 26 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 27

Table 27 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 27 is the same as compound 1 of Table 7 except that in compound 1 of Table 27 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 27 are the same as compounds 2 to 134 of Table 7, respectively, except that in the compounds of Table 27 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 28

Table 28 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonyl ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 28 is the same as compound 1 of Table 8 except that in compound 1 of Table 28 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 28 are the same as compounds 2 to 134 of Table 8, respectively, except that in the compounds of Table 28 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 29

Table 29 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxymethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 29 is the same as compound 1 of Table 9 except that in compound 1 of Table 29 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of methyl. Similarly, compounds 2 to 134 of Table 29 are the same as compounds 2 to 134 of Table 9, respectively, except that in the compounds of Table 29 R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

#### Table 30

Table 30 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxyethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *tert*-butyldimethylsilyloxymethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 30 is the same as compound 1 of Table 10 except that in compound 1 of Table 30 R<sub>5</sub> is



*tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 30 are the same as compounds 2 to 134 of Table 10, respectively, except that in the compounds of Table 30 R<sub>1</sub> is *tert*-butyldimethylsilyloxymethyl instead of hydroxymethyl.

5    Table 31

Table 31 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 31 is the same as compound 1 of Table 1 except that in compound 1 of Table 31 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 31 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 31 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

Table 32

Table 32 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1 for compounds 1 to 134. Thus compound 1 of Table 32 is the same as compound 1 of Table 2 except that in compound 1 of Table 32 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 32 are the same as compounds 2 to 134 of Table 2, respectively, except that in the compounds of Table 32 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

Table 33

Table 33 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is *n*-propyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, and R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 33 is the same as compound 1 of Table 3 except that in compound 1 of Table 33 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 33 are the same as compounds 2 to 134 of Table 3, respectively, except that in the compounds of Table 33 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

Table 34

Table 34 consists of 134 compounds of the general formula (1), where R<sub>1</sub> 2,2,2-trifluoromethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 34 is the same as compound 1 of Table 4 except that in compound 1 of Table 34 R<sub>5</sub> is 1-methoxyethyl instead of

hydroxymethyl. Similarly, compounds 2 to 134 of Table 34 are the same as compounds 2 to 134 of Table 4, respectively, except that in the compounds of Table 34 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

#### Table 35

5 Table 35 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is cyanomethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 35 is the same as compound 1 of Table 5 except that in compound 1 of Table 35 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 35 are the same as compounds 2 to 134  
10 of Table 5, respectively, except that in the compounds of Table 35 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

#### Table 36

Table 36 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is acetylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the  
15 values listed in Table 1. Thus compound 1 of Table 36 is the same as compound 1 of Table 6 except that in compound 1 of Table 36 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 36 are the same as compounds 2 to 134 of Table 6, respectively, except that in the compounds of Table 36 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

#### 20 Table 37

Table 37 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 37 is the same as compound 1 of Table 7 except that in compound 1 of Table 37 R<sub>5</sub> is 1-methoxyethyl  
25 instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 37 are the same as compounds 2 to 134 of Table 7, respectively, except that in the compounds of Table 37 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

#### Table 38

Table 38 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is  
30 methoxycarbonylethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 38 is the same as compound 1 of Table 8 except that in compound 1 of Table 38 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 38 are the same

as compounds 2 to 134 of Table 8, respectively, except that in the compounds of Table 38 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

#### Table 39

Table 39 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxymethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 39 is the same as compound 1 of Table 9 except that in compound 1 of Table 39 R<sub>5</sub> is 1-methoxyethyl instead of methyl. Similarly, compounds 2 to 134 of Table 39 are the same as compounds 2 to 134 of Table 9, respectively, except that in the compounds of Table 39 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

#### Table 40

Table 40 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxyethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 1-methoxyethyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 40 is the same as compound 1 of Table 10 except that in compound 1 of Table 40 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 40 are the same as compounds 2 to 134 of Table 10, respectively, except that in the compounds of Table 40 R<sub>5</sub> is 1-methoxyethyl instead of hydroxymethyl.

#### Table 41

Table 41 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 41 is the same as compound 1 of Table 1 except that in compound 1 of Table 41 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 41 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 41 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 42

Table 42 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1 for compounds 1 to 134. Thus compound 1 of Table 42 is the same as compound 1 of Table 2 except that in compound 1 of Table 42 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 42 are the same as

compounds 2 to 134 of Table 2, respectively, except that in the compounds of Table 42 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 43

Table 43 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is *n*-propyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, and R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 43 is the same as compound 1 of Table 3 except that in compound 1 of Table 43 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 43 are the same as compounds 2 to 134 of Table 3, respectively, except that in the compounds of Table 43 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 44

Table 44 consists of 134 compounds of the general formula (1), where R<sub>1</sub> 2,2,2-trifluoromethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 44 is the same as compound 1 of Table 4 except that in compound 1 of Table 44 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 44 are the same as compounds 2 to 134 of Table 4, respectively, except that in the compounds of Table 44 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 45

Table 45 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is cyanomethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 45 is the same as compound 1 of Table 5 except that in compound 1 of Table 45 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 45 are the same as compounds 2 to 134 of Table 5, respectively, except that in the compounds of Table 45 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 46

Table 46 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is acetylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 46 is the same as compound 1 of Table 6 except that in compound 1 of Table 46 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 46 are the same as compounds 2 to 134

of Table 6, respectively, except that in the compounds of Table 46 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 47

Table 47 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylmethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 47 is the same as compound 1 of Table 7 except that in compound 1 of Table 47 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 47 are the same as compounds 2 to 134 of Table 7, respectively, except that in the compounds of Table 47 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 48

Table 48 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is methoxycarbonylethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 48 is the same as compound 1 of Table 8 except that in compound 1 of Table 48 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 48 are the same as compounds 2 to 134 of Table 8, respectively, except that in the compounds of Table 48 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 49

Table 49 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxymethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 49 is the same as compound 1 of Table 9 except that in compound 1 of Table 49 R<sub>5</sub> is 3-cyanopropyl instead of methyl. Similarly, compounds 2 to 134 of Table 49 are the same as compounds 2 to 134 of Table 9, respectively, except that in the compounds of Table 49 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 50

Table 50 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is hydroxyethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-cyanopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 50 is the same as compound 1 of Table 10 except that in compound 1 of Table 50 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 50 are the same as

compounds 2 to 134 of Table 10, respectively, except that in the compounds of Table 50 R<sub>5</sub> is 3-cyanopropyl instead of hydroxymethyl.

#### Table 51

Table 51 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is *n*-propyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 51 is the same as compound 1 of Table 1 except that in compound 1 of Table 51 R<sub>5</sub> is *n*-propyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 51 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 51 R<sub>5</sub> is *n*-propyl instead of hydroxymethyl.

#### Table 52

Table 52 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-chloropropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 52 is the same as compound 1 of Table 1 except that in compound 1 of Table 52 R<sub>5</sub> is 3-chloropropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 52 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 52 R<sub>5</sub> is 3-chloropropyl instead of hydroxymethyl.

#### Table 53

Table 53 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-methylthiopropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 53 is the same as compound 1 of Table 1 except that in compound 1 of Table 53 R<sub>5</sub> is 3-methylthiopropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 53 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 53 R<sub>5</sub> is 3-methylthiopropyl instead of hydroxymethyl.

#### Table 54

Table 54 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-methanesulphinylpropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 54 is the same as compound 1 of Table 1 except that in compound 1 of Table 54 R<sub>5</sub> is 3-methanesulphinylpropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 54 are the same as

compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 54 R<sub>5</sub> is 3-methanesulphonylpropyl instead of hydroxymethyl.

#### Table 55

Table 55 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-methanesulphonylpropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 55 is the same as compound 1 of Table 1 except that in compound 1 of Table 55 R<sub>5</sub> is 3-methanesulphonylpropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 55 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 55 R<sub>5</sub> is 3-methanesulphonylpropyl instead of hydroxymethyl.

#### Table 56

Table 56 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-(1,2,4-triazol-1-yl)propyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 56 is the same as compound 1 of Table 1 except that in compound 1 of Table 56 R<sub>5</sub> is 3-(1,2,4-triazol-1-yl)propyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 56 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 56 R<sub>5</sub> is 3-(1,2,4-triazol-1-yl)propyl instead of hydroxymethyl.

#### Table 57

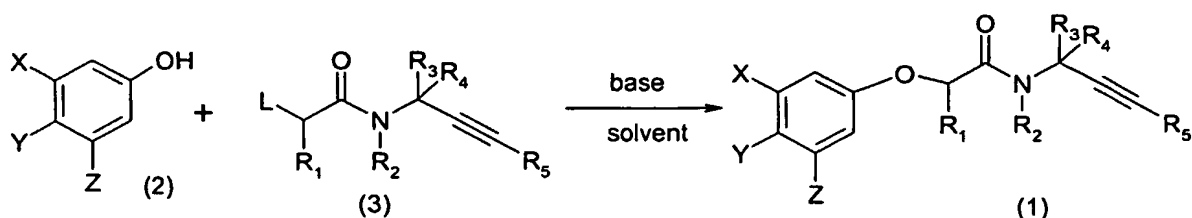
Table 57 consists of 134 compounds of the general formula (1), where R<sub>1</sub> is ethyl, R<sub>2</sub> is hydrogen, R<sub>3</sub> and R<sub>4</sub> are both methyl, R<sub>5</sub> is 3-methoxypropyl and X, Y and Z have the values listed in Table 1. Thus compound 1 of Table 57 is the same as compound 1 of Table 1 except that in compound 1 of Table 57 R<sub>5</sub> is 3-methoxypropyl instead of hydroxymethyl. Similarly, compounds 2 to 134 of Table 57 are the same as compounds 2 to 134 of Table 1, respectively, except that in the compounds of Table 57 R<sub>5</sub> is 3-methoxypropyl instead of hydroxymethyl.

The compounds of formula (1) may be prepared as outlined in Schemes 1 to 7 below in which X, Y, Z, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> have the meanings given above, R is C<sub>1-4</sub> alkyl, R<sub>6</sub> and R<sub>7</sub> are H or methyl but not both methyl, L is a leaving group such as a halide, for example iodide, an alkyl or aryl sulphonyloxy group, for example methylsulphonyloxy and tosyloxy or a triflate, Hal is halogen, R<sub>a</sub> is hydrogen or C<sub>1-3</sub> alkyl, R<sub>b</sub> is hydrogen or C<sub>1-3</sub> alkyl, provided that the total number of carbon atoms in R<sub>a</sub>

and  $R_b$  do not exceed three,  $R_c$  is  $C_{1-6}$  alkyl, optionally substituted benzyl or optionally substituted thienylmethyl and  $R_d$  has the meaning ascribed to it in the text.

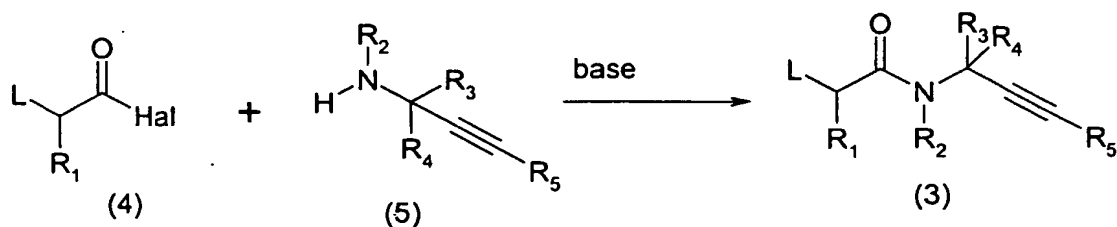
As shown in Scheme 1, the compounds of general formula (1) may be prepared by reacting a phenol of the general formula (2) with a compound of the general formula (3) in the presence of a base in a suitable solvent. Typical solvents include *N,N*-dimethylformamide and *N*-methylpyrrolidin-2-one. Suitable bases include potassium carbonate, sodium hydride or diisopropylethylamine. Phenols of the general formula (2) are either commercially available or are known in the literature or may be prepared from known compounds by standard procedures.

#### 10 Scheme 1



As shown in Scheme 2, compounds of general formula (3) may be prepared by reacting an amine of the general formula (5) with an acid halide of the general formula (4), or the corresponding acid anhydride, in the presence of a suitable inorganic or organic base, such as potassium carbonate, sodium hydride or diisopropylethylamine, in a solvent such as dichloromethane or tetrahydrofuran.

#### Scheme 2



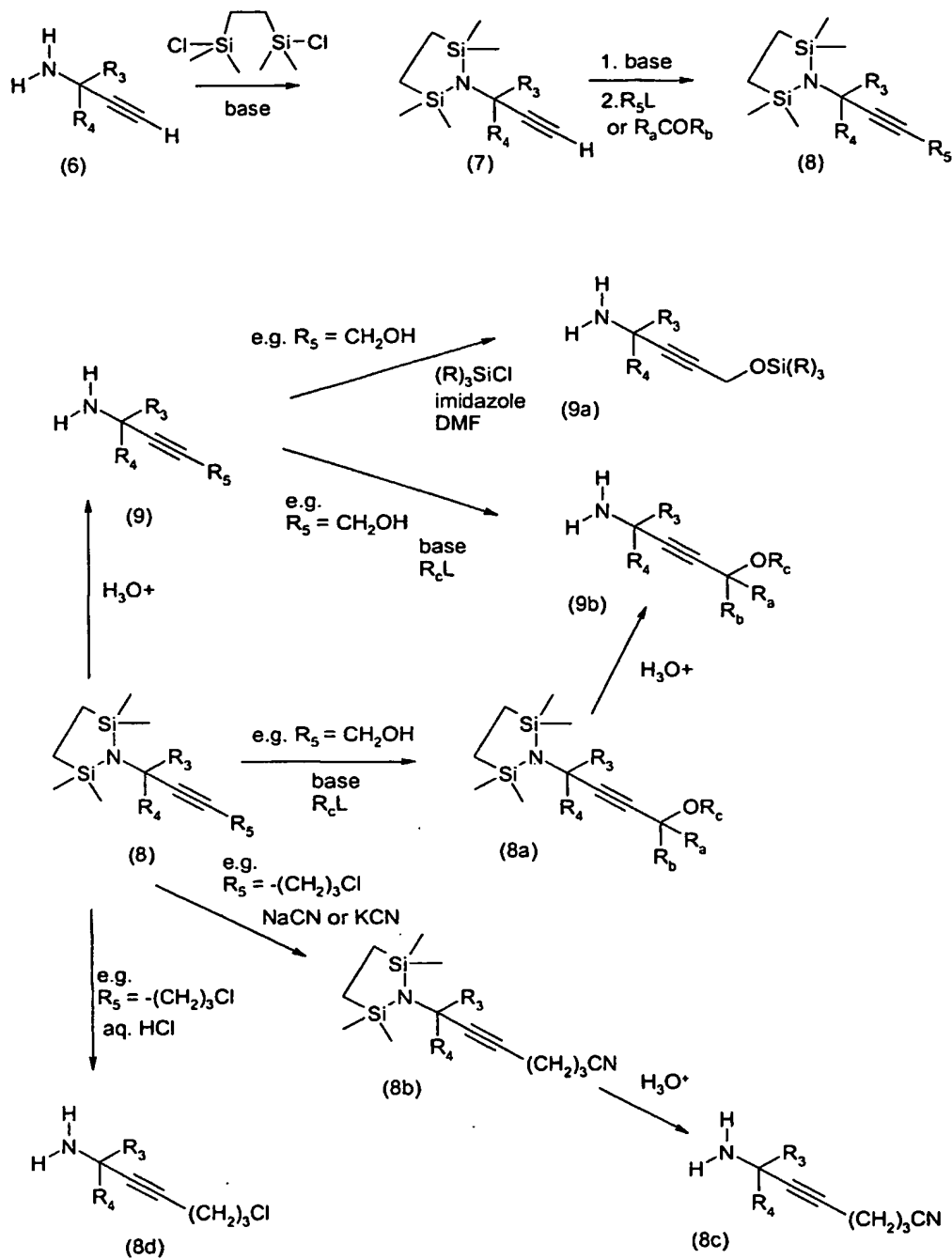
As shown in Scheme 3, amines of the general formula (5), wherein  $R_2$  is H, correspond to amines of the general formula (9) and may be prepared by alkylation of a silyl-protected aminoalkyne of the general formula (7) using a suitable base, such as *n*-butyl lithium, followed by reaction with a suitable alkylating reagent  $R_5L$ , such as an alkyl iodide, for example, methyl iodide, to form an alkylated compound of the general formula (8). In a similar procedure, a silyl-protected aminoalkyne of the general formula



(7) may be reacted with a carbonyl derivative  $R_aCOR_b$ , for example formaldehyde, using a suitable base, such as *n*-butyl lithium, to provide an aminoalkyne (8) containing a hydroxyalkyl moiety. The silyl protecting group may then be removed from a compound of the general formula (8) with, for example, an aqueous acid to form an aminoalkyne of the general formula (9). Aminoalkynes of the general formula (9) may be further derivatised, for instance when  $R_5$  is a hydroxyalkyl group, for example, by reacting a compound of the general formula (9) with a silylating agent  $(R)_3SiCl$ , for example *t*-butyldimethylsilyl chloride, to give a derivative silylated on oxygen of the general formula (9a). In addition, a compound of the general formula (9) may be treated with a base, such as sodium hydride or potassium *bis*(trimethylsilyl)amide followed by a compound  $R_cL$  to give a compound of the general formula (9b). In an alternative sequence, a compound of general formula (8) may be treated with a base, such as sodium or potassium *bis*(trimethylsilyl)amide, followed by a compound  $R_cL$ , where L represents a halogen or sulphonate ester such as  $OSO_2Me$ , or  $OSO_2$ -4-tolyl, for example ethyl iodide, to give compounds of the general formula (8a), which, after removal of the silyl protecting group, give compounds of the general formula (9b).

Compounds of general formula (8), where  $R_5$  is, for example, 3-chloropropyl can be reacted with a metal cyanide salt, such as sodium cyanide, to give compounds of general formula (8b), which can then be hydrolysed, with for example an aqueous acid, to give the amines of general formula (8c). Compounds of general formula (8), where  $R_5$  is, for example, 3-chloropropyl can be hydrolysed, with for example an aqueous acid, to give amines of general formula (8d).

Scheme 3



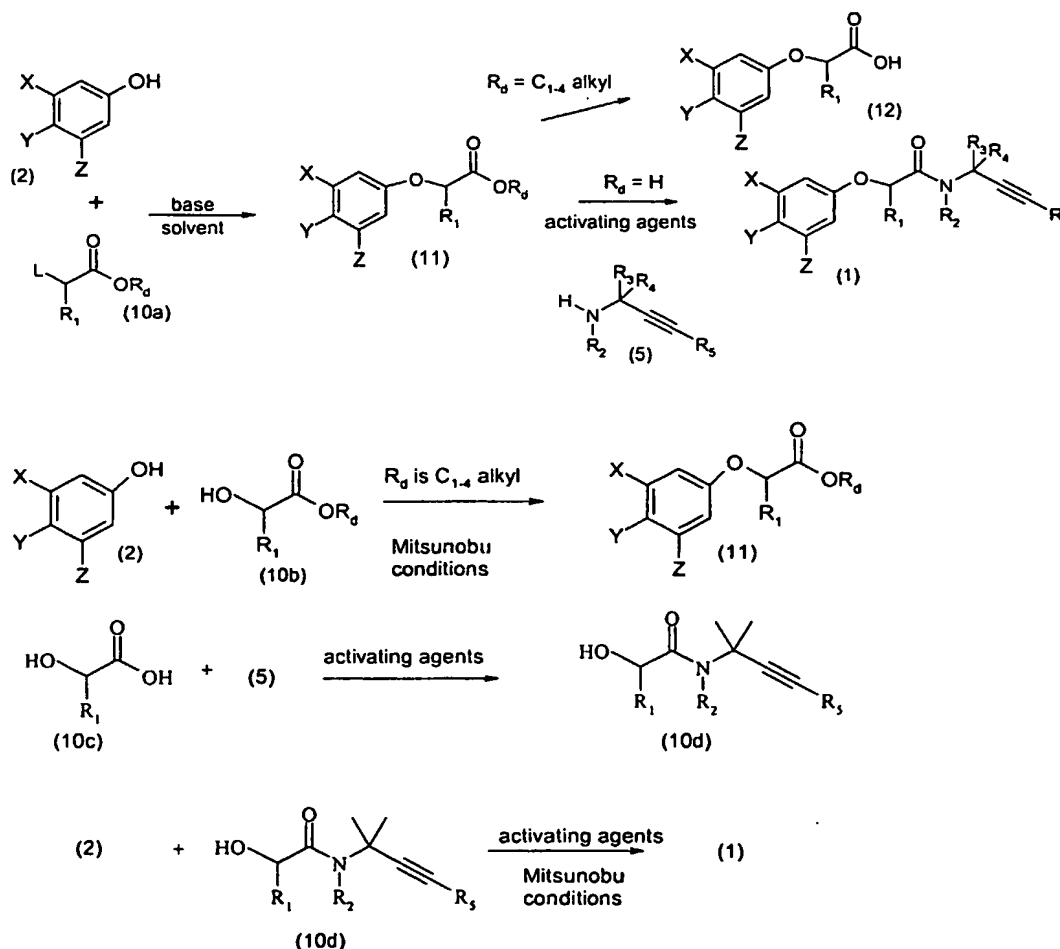
Silyl-protected aminoalkynes of the general formula (7) may be obtained by  
 5 reacting amines of general formula (6) with 1,2-bis-(chlorodimethylsilyl)ethane in the  
 presence of a suitable base, such as a tertiary organic amine base, for example,  
 triethylamine.

Amines of the general formula (6) are either commercially available or may be prepared by standard literature methods (see, for example, EP-A-0834498).

Alternatively, as shown in Scheme 4, compounds of the general formula (1) may be prepared by condensing a compound of the general formula (11), wherein  $R_d$  is H with an amine of the general formula (5) using suitable activating reagents such as 1-hydroxy-benzotriazole and *N*-(3-dimethylaminopropyl)-*N'*-ethyl-carbodiimide hydrochloride.

Where  $R_2$  is other than hydrogen, the  $R_2$  group may be introduced into an aminoalkyne of the general formula (9) by known techniques to form an amine of the general formula (5).

#### 10 Scheme 4



Compounds of the general formula (12) may be prepared by the hydrolysis of the corresponding esters of general formula (11), wherein  $R_d$  is  $C_{1-4}$  alkyl, using known techniques. The esters of the general formula (11), wherein  $R_d$  is  $C_{1-4}$  alkyl and also acids

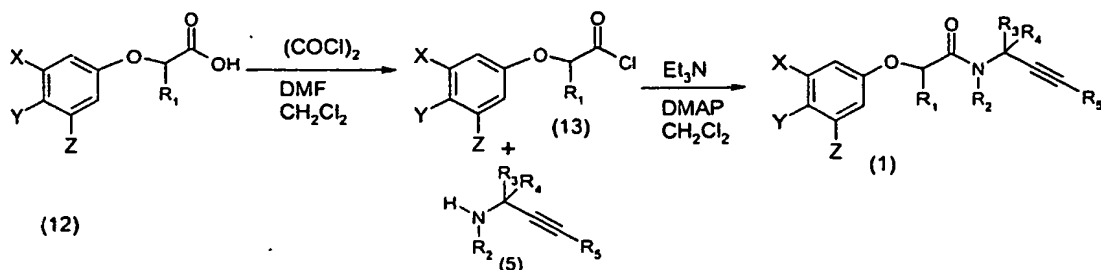
of the general formula (11), wherein  $R_d$  is H, may be prepared by reacting a compound of the general formula (2) with an ester or acid of the general formula (10a) in the presence of a suitable base, such as potassium carbonate or sodium hydride, in a suitable solvent, such as *N,N*-dimethylformamide. The esters or acids of the general formula (10a) are  
5 either commercially available or may be prepared by standard literature methods from commercially available materials.

Alternatively, as shown in Scheme 4, compounds of the general formula (11) may be prepared under Mitsunobu conditions by reacting a compound of the general formula (2) with a compound of the general formula (10b), wherein  $R_d$  is  $C_{1-4}$  alkyl, using a  
10 phosphine, such as triphenyl phosphine, and an azoester, such as diethyl azodicarboxylate.

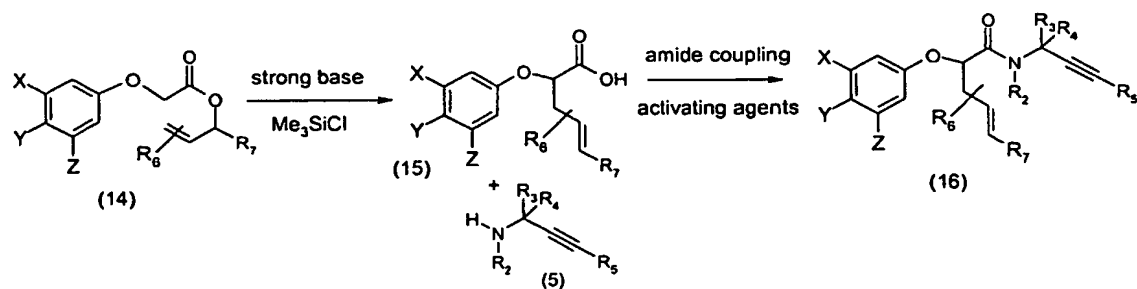
Similarly, compounds of the general formula (1) may be prepared by reacting a compound of general formula (10d) with a compound of the general formula (2) under Mitsunobu conditions using a phosphine, such as triphenyl phosphine, and an azoester,  
15 such as diethyl azodicarboxylate. Compounds of general formula (10d) may be prepared from a compound of general formula (10c) and an amine of general formula (5) using suitable activating reagents such as 1-hydroxybenzotriazole and *N*-(3-dimethylamino-propyl)-*N'*-ethyl-carbodiimide hydrochloride. Compounds (10b) and (10c) are either known compounds or may be made from known compounds.

20 In another method, the compounds of the general formula (1) may be prepared by reacting an acid halide of the general formula (13) with an amine of the general formula (5) in a suitable solvent, such as dichloromethane, in the presence of a tertiary amine, such as triethylamine, and an activating agent, such as 4-dimethylaminopyridine.

As shown in Scheme 5, an acid halide of the general formula (13) may be  
25 prepared by chlorinating a compound of the general formula (12) with a suitable chlorinating agent, such as oxalyl chloride, in a suitable solvent, such as dichloromethane, and in the presence of, for example, *N,N*-dimethylformamide. The compounds of the general formula (12) correspond to the compounds of general formula (11), wherein  $R_d$  is H.

Scheme 5

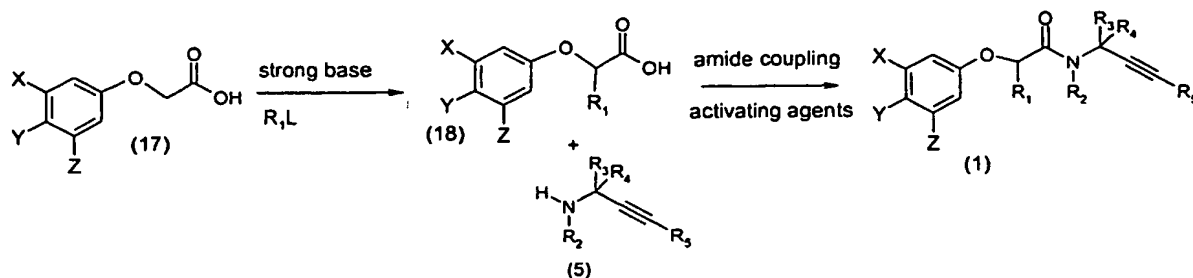
As shown in Scheme 6, compounds of the general formula (1), where  $R_1$  is a  $C_{3-4}$  alkenyl group, may be prepared from compounds of the general formula (14). Compounds of the general formula (14) are treated with a strong base, such as lithium bis(trimethylsilyl)amide, at between  $-78^\circ\text{C}$  and room temperature but preferably at  $-78^\circ\text{C}$ , and then reacted with a trialkylsilyl chloride, such as trimethylsilyl chloride or trialkylsilyl triflate  $R_3\text{SiOSO}_2\text{CF}_3$ , and allowed to warm to ambient temperature. The resultant acids of the general formula (15) obtained after hydrolysis can be condensed with amines of the general formula (5) to give the compounds of the general formula (16), using suitable activating reagents such as 1-hydroxybenzotriazole and *N*-(3-dimethylaminopropyl)-*N'*-ethyl-carbodiimide hydrochloride.

Scheme 6

Compounds of the general formula (1), wherein  $R_1$  is a  $C_{1-4}$  alkyl group,  $C_{3-4}$  alkenyl group or  $C_{3-4}$  alkynyl group, may be prepared as shown in Scheme 7. Phenoxyacetic acids of the general formula (17) are treated with at least two equivalents of a strong base such as lithium diisopropylamide, in a suitable solvent such tetrahydrofuran, at a temperature of between  $-78^\circ\text{C}$  and  $0^\circ\text{C}$ , but preferably at  $-78^\circ\text{C}$ , followed by a compound  $R_1\text{L}$ , where L is a leaving group such as a halide, mesylate or triflate, and then allowed to warm up to ambient temperature to give, after acidification, phenoxyalkyl carboxylic acids of the general formula (18). Phenoxyalkyl carboxylic acids of the general formula (18) can be condensed with the amines of the general formula (5) to give

the compounds of the general formula (1), using suitable activating reagents such as 1-hydroxybenzotriazole and *N*-(3-dimethylaminopropyl)-*N'*-ethyl-carbodiimide hydrochloride.

### Scheme 7

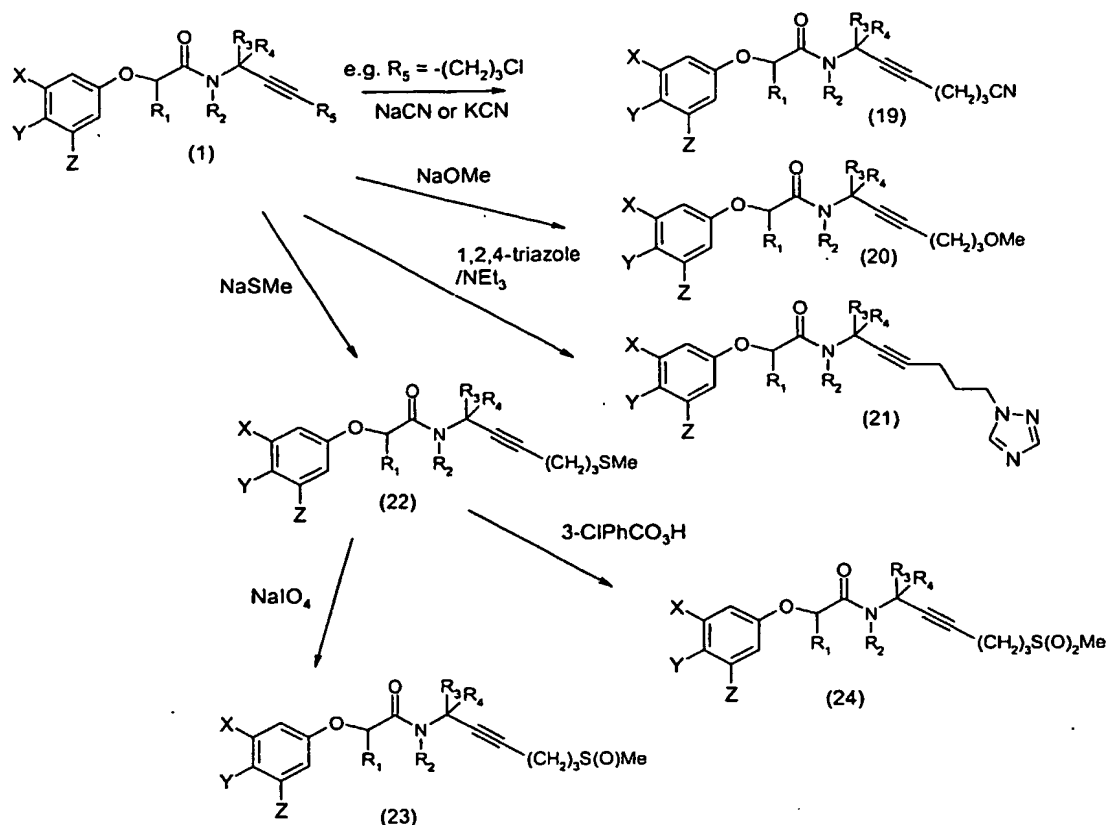


5

As shown in Scheme 8, compounds of general formula (1), where R<sub>5</sub> is for example 3-chloropropyl, can be reacted with various nucleophiles such as a metal cyanide salt, for example sodium cyanide, to give compounds of general formula (19), with metal alkoxides, for example sodium methoxide, to give compounds of general formula (20), with 1,2,4-triazole in the presence of base such as triethylamine to give compounds of general formula (21) and with metal thioalkoxides, for example sodium methanethiolate, to give compounds of general formula (22). Compounds of general formula (22) can be treated with oxidising agents such as sodium periodate, to give sulphoxides of general formula (23), or with oxidising agents such as 3-chloroperbenzoic acid, to give sulphones of general formula (24).

15

Scheme 8



Other compounds of the invention may be prepared by transforming the substituents in the compounds of general formula (1) using known procedures e.g. by the alkylation of compounds of formula (1), wherein R<sub>2</sub> is H or R<sub>5</sub> is H.

The compounds of formula (1) are active fungicides and may be used to control one or more of the following pathogens: *Pyricularia oryzae* (*Magnaporthe grisea*) on rice and wheat and other *Pyricularia* spp. on other hosts; *Puccinia trititica* (or *recondita*), *Puccinia striiformis* and other rusts on wheat, *Puccinia hordei*, *Puccinia striiformis* and other rusts on barley, and rusts on other hosts (for example turf, rye, coffee, pears, apples, peanuts, sugar beet, vegetables and ornamental plants); *Erysiphe cichoracearum* on cucurbits (for example melon); *Blumeria* (or *Erysiphe*) *graminis* (powdery mildew) on barley, wheat, rye and turf and other powdery mildews on various hosts, such as *Sphaerotheca macularis* on hops, *Sphaerotheca fusca* (*Sphaerotheca fuliginea*) on cucurbits (for example cucumber), *Leveillula taurica* on tomatoes, aubergine and green pepper, *Podosphaera leucotricha* on apples and *Uncinula necator* on vines; *Cochliobolus* spp., *Helminthosporium* spp., *Drechslera* spp. (*Pyrenophora* spp.), *Rhynchosporium* spp., *Mycosphaerella graminicola* (*Septoria tritici*) and *Phaeosphaeria nodorum*.

(*Stagonospora nodorum* or *Septoria nodorum*), *Pseudocercospora herpotrichoides* and *Gaeumannomyces graminis* on cereals (for example wheat, barley, rye), turf and other hosts; *Cercospora arachidicola* and *Cercosporidium personatum* on peanuts and other *Cercospora* spp. on other hosts, for example sugar beet, bananas, soya beans and rice;

5 *Botrytis cinerea* (grey mould) on tomatoes, strawberries, vegetables, vines and other hosts and other *Botrytis* spp. on other hosts; *Alternaria* spp. on vegetables (for example carrots), oil-seed rape, apples, tomatoes, potatoes, cereals (for example wheat) and other hosts; *Venturia* spp. (including *Venturia inaequalis* (scab)) on apples, pears, stone fruit, tree nuts and other hosts; *Cladosporium* spp. on a range of hosts including cereals (for

10 example wheat) and tomatoes; *Monilinia* spp. on stone fruit, tree nuts and other hosts; *Didymella* spp. on tomatoes, turf, wheat, cucurbits and other hosts; *Phoma* spp. on oil-seed rape, turf, rice, potatoes, wheat and other hosts; *Aspergillus* spp. and *Aureobasidium* spp. on wheat, lumber and other hosts; *Ascochyta* spp. on peas, wheat, barley and other hosts; *Stemphylium* spp. (*Pleospora* spp.) on apples, pears, onions and

15 other hosts; summer diseases (for example bitter rot (*Glomerella cingulata*), black rot or frog-eye leaf spot (*Botryosphaeria obtusa*), Brooks fruit spot (*Mycosphaerella pomi*), Cedar apple rust (*Gymnosporangium juniperi-virginianae*), sooty blotch (*Gloeodes pomigena*), flyspeck (*Schizothyrium pomi*) and white rot (*Botryosphaeria dothidea*)) on apples and pears; *Plasmopara viticola* on vines; other downy mildews, such as *Bremia*

20 *lactucae* on lettuce, *Peronospora* spp. on soybeans, tobacco, onions and other hosts, *Pseudoperonospora humuli* on hops and *Pseudoperonospora cubensis* on cucurbits; *Pythium* spp. (including *Pythium ultimum*) on turf and other hosts; *Phytophthora infestans* on potatoes and tomatoes and other *Phytophthora* spp. on vegetables, strawberries, avocado, pepper, ornamentals, tobacco, cocoa and other hosts;

25 *Thanatephorus cucumeris* on rice and turf and other *Rhizoctonia* spp. on various hosts such as wheat and barley, peanuts, vegetables, cotton and turf; *Sclerotinia* spp. on turf, peanuts, potatoes, oil-seed rape and other hosts; *Sclerotium* spp. on turf, peanuts and other hosts; *Gibberella fujikuroi* on rice; *Colletotrichum* spp. on a range of hosts including turf, coffee and vegetables; *Laetisaria fuciformis* on turf; *Mycosphaerella* spp. on bananas,

30 peanuts, citrus, pecans, papaya and other hosts; *Diaporthe* spp. on citrus, soybean, melon, pears, lupin and other hosts; *Elsinoe* spp. on citrus, vines, olives, pecans, roses and other hosts; *Verticillium* spp. on a range of hosts including hops, potatoes and tomatoes; *Pyrenopeziza* spp. on oil-seed rape and other hosts; *Oncobasidium theobromae* on cocoa



causing vascular streak dieback; *Fusarium* spp., *Typhula* spp., *Microdochium nivale*, *Ustilago* spp., *Urocystis* spp., *Tilletia* spp. and *Claviceps purpurea* on a variety of hosts but particularly wheat, barley, turf and maize; *Ramularia* spp. on sugar beet, barley and other hosts; post-harvest diseases particularly of fruit (for example *Penicillium digitatum*,  
5 *Penicillium italicum* and *Trichoderma viride* on oranges, *Colletotrichum musae* and *Gloeosporium musarum* on bananas and *Botrytis cinerea* on grapes); other pathogens on vines, notably *Eutypa lata*, *Guignardia bidwellii*, *Phellinus igniarius*, *Phomopsis viticola*, *Pseudopeziza tracheiphila* and *Stereum hirsutum*; other pathogens on trees (for example *Lophodermium seeditiosum*) or lumber, notably *Cephaloascus fragrans*, *Ceratocystis* spp.,  
10 *Ophiostoma piceae*, *Penicillium* spp., *Trichoderma pseudokoningii*, *Trichoderma viride*, *Trichoderma harzianum*, *Aspergillus niger*, *Leptographium lindbergi* and *Aureobasidium pullulans*; and fungal vectors of viral diseases (for example *Polymyxa graminis* on cereals as the vector of barley yellow mosaic virus (BYMV) and *Polymyxa betae* on sugar beet as the vector of rhizomania).

15 The compounds of formula (I) show particularly good activity against the Oomycete class of pathogens such as *Phytophthora infestans*, *Plasmopara* species, e.g. *Plasmopara viticola* and *Pythium* species e.g. *Pythium ultimum*.

A compound of formula (1) may move acropetally, basipetally or locally in plant tissue to be active against one or more fungi. Moreover, a compound of formula (1) may  
20 be volatile enough to be active in the vapour phase against one or more fungi on the plant.

The invention therefore provides a method of combating or controlling phytopathogenic fungi which comprises applying a fungicidally effective amount of a compound of formula (1), or a composition containing a compound of formula (1), to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other plant  
25 growth medium, e.g. nutrient solution.

The term "plant" as used herein includes seedlings, bushes and trees. Furthermore, the fungicidal method of the invention includes protectant, curative, systemic, eradicant and antisporeulant treatments.

The compounds of formula (1) are preferably used for agricultural, horticultural  
30 and turfgrass purposes in the form of a composition.

In order to apply a compound of formula (1) to a plant, to a seed of a plant, to the locus of the plant or seed or to soil or any other growth medium, a compound of formula (1) is usually formulated into a composition which includes, in addition to the compound

of formula (1), a suitable inert diluent or carrier and, optionally, a surface active agent (SFA). SFAs are chemicals which are able to modify the properties of an interface (for example, liquid/solid, liquid/air or liquid/liquid interfaces) by lowering the interfacial tension and thereby leading to changes in other properties (for example dispersion, emulsification and wetting). It is preferred that all compositions (both solid and liquid formulations) comprise, by weight, 0.0001 to 95%, more preferably 1 to 85%, for example 5 to 60%, of a compound of formula (1). The composition is generally used for the control of fungi such that a compound of formula (1) is applied at a rate of from 0.1g to 10kg per hectare, preferably from 1g to 6kg per hectare, more preferably from 1g to 1kg per hectare.

When used in a seed dressing, a compound of formula (1) is used at a rate of 0.0001g to 10g (for example 0.001g or 0.05g), preferably 0.005g to 10g, more preferably 0.005g to 4g, per kilogram of seed.

In another aspect the present invention provides a fungicidal composition comprising a fungicidally effective amount of a compound of formula (1) and a suitable carrier or diluent therefor.

In a still further aspect the invention provides a method of combating and controlling fungi at a locus, which comprises treating the fungi, or the locus of the fungi with a fungicidally effective amount of a composition comprising a compound of formula (1).

The compositions can be chosen from a number of formulation types, including dustable powders (DP), soluble powders (SP), water soluble granules (SG), water dispersible granules (WG), wettable powders (WP), granules (GR) (slow or fast release), soluble concentrates (SL), oil miscible liquids (OL), ultra low volume liquids (UL), emulsifiable concentrates (EC), dispersible concentrates (DC), emulsions (both oil in water (EW) and water in oil (EO)), micro-emulsions (ME), suspension concentrates (SC), aerosols, fogging/smoke formulations, capsule suspensions (CS) and seed treatment formulations. The formulation type chosen in any instance will depend upon the particular purpose envisaged and the physical, chemical and biological properties of the compound of formula (1).

Dustable powders (DP) may be prepared by mixing a compound of formula (1) with one or more solid diluents (for example natural clays, kaolin, pyrophyllite, bentonite, alumina, montmorillonite, kieselguhr, chalk, diatomaceous earths, calcium

phosphates, calcium and magnesium carbonates, sulphur, lime, flours, talc and other organic and inorganic solid carriers) and mechanically grinding the mixture to a fine powder.

Soluble powders (SP) may be prepared by mixing a compound of formula (1) with one or more water-soluble inorganic salts (such as sodium bicarbonate, sodium carbonate or magnesium sulphate) or one or more water-soluble organic solids (such as a polysaccharide) and, optionally, one or more wetting agents, one or more dispersing agents or a mixture of said agents to improve water dispersibility/solubility. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water soluble granules (SG).

Wettable powders (WP) may be prepared by mixing a compound of formula (1) with one or more solid diluents or carriers, one or more wetting agents and, preferably, one or more dispersing agents and, optionally, one or more suspending agents to facilitate the dispersion in liquids. The mixture is then ground to a fine powder. Similar compositions may also be granulated to form water dispersible granules (WG).

Granules (GR) may be formed either by granulating a mixture of a compound of formula (1) and one or more powdered solid diluents or carriers, or from pre-formed blank granules by absorbing a compound of formula (1) (or a solution thereof, in a suitable agent) in a porous granular material (such as pumice, attapulgite clays, fuller's earth, kieselguhr, diatomaceous earths or ground corn cobs) or by adsorbing a compound of formula (1) (or a solution thereof, in a suitable agent) on to a hard core material (such as sands, silicates, mineral carbonates, sulphates or phosphates) and drying if necessary. Agents which are commonly used to aid absorption or adsorption include solvents (such as aliphatic and aromatic petroleum solvents, alcohols, ethers, ketones and esters) and sticking agents (such as polyvinyl acetates, polyvinyl alcohols, dextrans, sugars and vegetable oils). One or more other additives may also be included in granules (for example an emulsifying agent, wetting agent or dispersing agent).

Dispersible Concentrates (DC) may be prepared by dissolving a compound of formula (1) in water or an organic solvent, such as a ketone, alcohol or glycol ether. These solutions may contain a surface active agent (for example to improve water dilution or prevent crystallisation in a spray tank).

Emulsifiable concentrates (EC) or oil-in-water emulsions (EW) may be prepared by dissolving a compound of formula (1) in an organic solvent (optionally containing one

or more wetting agents, one or more emulsifying agents or a mixture of said agents). Suitable organic solvents for use in ECs include aromatic hydrocarbons (such as alkylbenzenes or alkylnaphthalenes, exemplified by SOLVESSO 100, SOLVESSO 150 and SOLVESSO 200; SOLVESSO is a Registered Trade Mark), ketones (such as  
5 cyclohexanone or methylcyclohexanone), alcohols (such as benzyl alcohol, furfuryl alcohol or butanol), *N*-alkylpyrrolidones (such as *N*-methylpyrrolidone or *N*-octylpyrrolidone), dimethyl amides of fatty acids (such as C<sub>8</sub>-C<sub>10</sub> fatty acid dimethylamide) and chlorinated hydrocarbons. An EC product may spontaneously emulsify on addition to water, to produce an emulsion with sufficient stability to allow  
10 spray application through appropriate equipment. Preparation of an EW involves obtaining a compound of formula (1) either as a liquid (if it is not a liquid at room temperature, it may be melted at a reasonable temperature, typically below 70°C) or in solution (by dissolving it in an appropriate solvent) and then emulsifying the resultant liquid or solution into water containing one or more SFAs, under high shear, to produce  
15 an emulsion. Suitable solvents for use in EWs include vegetable oils, chlorinated hydrocarbons (such as chlorobenzenes), aromatic solvents (such as alkylbenzenes or alkylnaphthalenes) and other appropriate organic solvents which have a low solubility in water.

Microemulsions (ME) may be prepared by mixing water with a blend of one or  
20 more solvents with one or more SFAs, to produce spontaneously a thermodynamically stable isotropic liquid formulation. A compound of formula (1) is present initially in either the water or the solvent/SFA blend. Suitable solvents for use in MEs include those hereinbefore described for use in ECs or in EWs. An ME may be either an oil-in-water or a water-in-oil system (which system is present may be determined by conductivity  
25 measurements) and may be suitable for mixing water-soluble and oil-soluble pesticides in the same formulation. An ME is suitable for dilution into water, either remaining as a microemulsion or forming a conventional oil-in-water emulsion.

Suspension concentrates (SC) may comprise aqueous or non-aqueous suspensions of finely divided insoluble solid particles of a compound of formula (1). SCs may be  
30 prepared by ball or bead milling the solid compound of formula (1) in a suitable medium, optionally with one or more dispersing agents, to produce a fine particle suspension of the compound. One or more wetting agents may be included in the composition and a suspending agent may be included to reduce the rate at which the particles settle.

Alternatively, a compound of formula (1) may be dry milled and added to water, containing agents hereinbefore described, to produce the desired end product.

Aerosol formulations comprise a compound of formula (1) and a suitable propellant (for example *n*-butane). A compound of formula (1) may also be dissolved or  
5 dispersed in a suitable medium (for example water or a water miscible liquid, such as *n*-propanol) to provide compositions for use in non-pressurised, hand-actuated spray pumps.

A compound of formula (1) may be mixed in the dry state with a pyrotechnic mixture to form a composition suitable for generating, in an enclosed space, a smoke  
10 containing the compound.

Capsule suspensions (CS) may be prepared in a manner similar to the preparation of EW formulations but with an additional polymerisation stage such that an aqueous dispersion of oil droplets is obtained, in which each oil droplet is encapsulated by a polymeric shell and contains a compound of formula (1) and, optionally, a carrier or  
15 diluent therefor. The polymeric shell may be produced by either an interfacial polycondensation reaction or by a coacervation procedure. The compositions may provide for controlled release of the compound of formula (1) and they may be used for seed treatment. A compound of formula (1) may also be formulated in a biodegradable polymeric matrix to provide a slow, controlled release of the compound.

20 A composition may include one or more additives to improve the biological performance of the composition (for example by improving wetting, retention or distribution on surfaces; resistance to rain on treated surfaces; or uptake or mobility of a compound of formula (1)). Such additives include surface active agents, spray additives based on oils, for example certain mineral oils or natural plant oils (such as soy bean and  
25 rape seed oil), and blends of these with other bio-enhancing adjuvants (ingredients which may aid or modify the action of a compound of formula (1)).

A compound of formula (1) may also be formulated for use as a seed treatment, for example as a powder composition, including a powder for dry seed treatment (DS), a water soluble powder (SS) or a water dispersible powder for slurry treatment (WS), or as  
30 a liquid composition, including a flowable concentrate (FS), a solution (LS) or a capsule suspension (CS). The preparations of DS, SS, WS, FS and LS compositions are very similar to those of, respectively, DP, SP, WP, SC and DC compositions described above.

Compositions for treating seed may include an agent for assisting the adhesion of the composition to the seed (for example a mineral oil or a film-forming barrier).

Wetting agents, dispersing agents and emulsifying agents may be SFAs of the cationic, anionic, amphoteric or non-ionic type.

5           Suitable SFAs of the cationic type include quaternary ammonium compounds (for example cetyltrimethyl ammonium bromide), imidazolines and amine salts.

          Suitable anionic SFAs include alkali metals salts of fatty acids, salts of aliphatic monoesters of sulphuric acid (for example sodium lauryl sulphate), salts of sulphonated aromatic compounds (for example sodium dodecylbenzenesulphonate, calcium  
10   dodecylbenzenesulphonate, butylnaphthalene sulphonate and mixtures of sodium di-*isopropyl*- and *tri-isopropyl*-naphthalene sulphonates), ether sulphates, alcohol ether sulphates (for example sodium laureth-3-sulphate), ether carboxylates (for example sodium laureth-3-carboxylate), phosphate esters (products from the reaction between one or more fatty alcohols and phosphoric acid (predominately mono-esters) or phosphorus  
15   pentoxide (predominately di-esters), for example the reaction between lauryl alcohol and tetraphosphoric acid; additionally these products may be ethoxylated), sulphosuccinamates, paraffin or olefine sulphonates, taurates and lignosulphonates.

          Suitable SFAs of the amphoteric type include betaines, propionates and glycines.

20           Suitable SFAs of the non-ionic type include condensation products of alkylene oxides, such as ethylene oxide, propylene oxide, butylene oxide or mixtures thereof, with fatty alcohols (such as oleyl alcohol or cetyl alcohol) or with alkylphenols (such as octylphenol, nonylphenol or octylcresol); partial esters derived from long chain fatty acids or hexitol anhydrides; condensation products of said partial esters with ethylene oxide;  
25   block polymers (comprising ethylene oxide and propylene oxide); alkanolamides; simple esters (for example fatty acid polyethylene glycol esters); amine oxides (for example lauryl dimethyl amine oxide); and lecithins.

          Suitable suspending agents include hydrophilic colloids (such as polysaccharides, polyvinylpyrrolidone or sodium carboxymethylcellulose) and swelling clays (such as  
30   bentonite or attapulgite).

          A compound of formula (1) may be applied by any of the known means of applying fungicidal compounds. For example, it may be applied, formulated or unformulated, to any part of the plant, including the foliage, stems, branches or roots, to

the seed before it is planted or to other media in which plants are growing or are to be planted (such as soil surrounding the roots, the soil generally, paddy water or hydroponic culture systems), directly or it may be sprayed on, dusted on, applied by dipping, applied as a cream or paste formulation, applied as a vapour or applied through distribution or  
5 incorporation of a composition (such as a granular composition or a composition packed in a water-soluble bag) in soil or an aqueous environment.

A compound of formula (1) may also be injected into plants or sprayed onto vegetation using electrodynamic spraying techniques or other low volume methods, or applied by land or aerial irrigation systems.

10 Compositions for use as aqueous preparations (aqueous solutions or dispersions) are generally supplied in the form of a concentrate containing a high proportion of the active ingredient, the concentrate being added to water before use. These concentrates, which may include DCs, SCs, ECs, EWs, MEs SGs, SPs, WPs, WGs and CSs, are often required to withstand storage for prolonged periods and, after such storage, to be capable  
15 of addition to water to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. Such aqueous preparations may contain varying amounts of a compound of formula (1) (for example 0.0001 to 10%, by weight) depending upon the purpose for which they are to be used.

20 A compound of formula (1) may be used in mixtures with fertilisers (for example nitrogen-, potassium- or phosphorus-containing fertilisers). Suitable formulation types include granules of fertiliser. The mixtures suitably contain up to 25% by weight of the compound of formula (1).

The invention therefore also provides a fertiliser composition comprising a  
25 fertiliser and a compound of formula (1).

The compositions of this invention may contain other compounds having biological activity, for example micronutrients or compounds having similar or complementary fungicidal activity or which possess plant growth regulating, herbicidal, insecticidal, nematocidal or acaricidal activity.

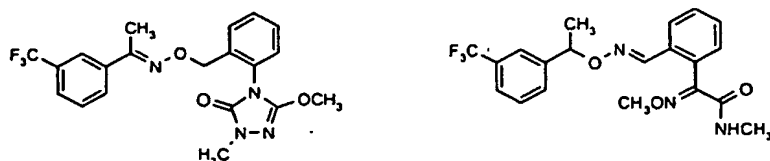
30 By including another fungicide, the resulting composition may have a broader spectrum of activity or a greater level of intrinsic activity than the compound of formula (1) alone. Further the other fungicide may have a synergistic effect on the fungicidal activity of the compound of formula (1).

The compound of formula (1) may be the sole active ingredient of the composition or it may be admixed with one or more additional active ingredients such as a pesticide, fungicide, synergist, herbicide or plant growth regulator where appropriate. An additional active ingredient may: provide a composition having a broader spectrum of activity or increased persistence at a locus; synergise the activity or complement the activity (for example by increasing the speed of effect or overcoming repellency) of the compound of formula (1); or help to overcome or prevent the development of resistance to individual components. The particular additional active ingredient will depend upon the intended utility of the composition.

Examples of fungicidal compounds which may be included in the composition of the invention are AC 382042 (*N*-(1-cyano-1,2-dimethylpropyl)-2-(2,4-dichlorophenoxy) propionamide), acibenzolar-S-methyl, alanycarb, aldimorph, anilazine, azaconazole, azafenidin, azoxystrobin, benalaxyl, benomyl, benthiavalicarb, biloxazol, bitertanol, blasticidin S, boscalid (new name for nicobifen), bromuconazole, bupirimate, captafol, captan, carbendazim, carbendazim chlorhydrate, carboxin, carpropamid, carvone, CGA 41396, CGA 41397, chinomethionate, chlorbenzthiazole, chlorothalonil, chlorozoline, clozylacon, copper containing compounds such as copper oxychloride, copper oxyquinolate, copper sulphate, copper tallate, and Bordeaux mixture, cyamidazosulfamid, cyazofamid (IKF-916), cyflufenamid, cymoxanil, cyproconazole, cyprodinil, debacarb, di-2-pyridyl disulphide 1,1'-dioxide, dichlofluanid, diclocymet, diclomezine, dicloran, diethofencarb, difenoconazole, difenzoquat, diflumetorim, *O,O*-di-*iso*-propyl-*S*-benzyl thiophosphate, dimefluazole, dimetconazole, dimethirimol, dimethomorph, dimoxystrobin, diniconazole, dinocap, dithianon, dodecyl dimethyl ammonium chloride, dodemorph, dodine, doguadine, edifenphos, epoxiconazole, ethaboxam, ethirimol, ethyl (*Z*)-*N*-benzyl-*N*-([methyl(methyl-thioethylideneaminooxycarbonyl)amino]thio)- $\beta$ -alaninate, etridiazole, famoxadone, fenamidone, fenarimol, fenbuconazole, fenfuram, fenhexamid, fenoxanil (AC 382042), fenpiclonil, fenpropidin, fenpropimorph, fentin acetate, fentin hydroxide, ferbam, ferimzone, fluazinam, fludioxonil, flumetover, flumorph, fluoroimide, fluoxastrobin, fluquinconazole, flusilazole, flusulfamide, flutolanil, flutriafol, folpet, fosetyl-aluminium, fuberidazole, furalaxyl, furametpyr, guazatine, hexaconazole, hydroxyisoxazole, hymexazole, imazalil, imibenconazole, iminoctadine, iminoctadine triacetate, ipconazole, iprobenfos, iprodione, iprovalicarb, isopropanyl butyl carbamate, isoprothiolane, kasugamycin, kresoxim-methyl, LY186054,



LY211795, LY 248908, mancozeb, maneb, mefenoxam, mepanipyrim, mepronil, metalaxyl, metalaxyl M, metconazole, metiram, metiram-zinc, metominostrobin, metrafenone, MON65500 (*N*-allyl-4,5-dimethyl-2-trimethylsilylthiophene-3-carboxamide), myclobutanil, NTN0301, neoasozin, nickel dimethyldithiocarbamate, 5 nitrothale-isopropyl, nuarimol, ofurace, organomercury compounds, orysastrobin, oxadixyl, oxasulfuron, oxolinic acid, oxpoconazole, oxycarboxin, pefurazoate, penconazole, pencycuron, phenazin oxide, phosphorus acids, phthalide, picoxystrobin, polyoxin D, polyram, probenazole, prochloraz, procymidone, propamocarb, propamocarb hydrochloride, propiconazole, propineb, propionic acid, proquinazid, prothioconazole, 10 pyraclostrobin, pyrazophos, pyrifenox, pyrimethanil, pyroquilon, pyroxyfur, pyrrolnitrin, quaternary ammonium compounds, quinomethionate, quinoxifen, quintozone, silthiofam (MON 65500), S-imazalil, simeconazole, sipconazole, sodium pentachlorophenate, spiroxamine, streptomycin, sulphur, tebuconazole, tecloftalam, tecnazene, tetraconazole, thiabendazole, thifluzamide, 2-(thiocyanomethylthio)benzothiazole, thiophanate-methyl, 15 thiram, tiadinil, timibenconazole, tolclofos-methyl, tolylfluanid, triadimefon, triadimenol, triazbutil, triazoxide, tricyclazole, tridemorph, trifloxystrobin, triflumizole, triforine, triticonazole, validamycin A, vapam, vinclozolin, XRD-563, zineb, ziram, zoxamide and compounds of the formulae:



20 The compounds of formula (1) may be mixed with soil, peat or other rooting media for the protection of plants against seed-borne, soil-borne or foliar fungal diseases.

Some mixtures may comprise active ingredients which have significantly different physical, chemical or biological properties such that they do not easily lend themselves to the same conventional formulation type. In these circumstances other formulation types 25 may be prepared. For example, where one active ingredient is a water insoluble solid and the other a water insoluble liquid, it may nevertheless be possible to disperse each active ingredient in the same continuous aqueous phase by dispersing the solid active ingredient as a suspension (using a preparation analogous to that of an SC) but dispersing the liquid active ingredient as an emulsion (using a preparation analogous to that of an EW). The 30 resultant composition is a suspoemulsion (SE) formulation.

The invention is illustrated by the following Examples in which the following abbreviations are used:

ml = millilitres

g = grammes

ppm = parts per million

M<sup>+</sup> = mass ion

s = singlet

d = doublet

br s = broad singlet

t = triplet

DMSO = dimethylsulphoxide

NMR = nuclear magnetic resonance

HPLC = high performance liquid chromatography

q = quartet

m = multiplet

ppm = parts per million

#### EXAMPLE 1

- 5 This Example illustrates the preparation of 2-(3,5-dichlorophenoxy)-*N*-(1-*tert*-butyl-dimethylsilyloxy-4-methylpent-2-yn-4-yl) butyramide (Compound No. 4 in Table 21)

##### Stage 1: Preparation of 4-amino-1-hydroxy-4-methylpent-2-yne hydrochloride

##### Step 1

- 1-(1,1-Dimethyl-2-propynyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane  
10 (prepared as described below; 22.6g) in dry tetrahydrofuran (250ml) was cooled to -50°C under an atmosphere of nitrogen with stirring and a solution of *n*-butyl lithium ( 44ml, 2.5M solution in hexanes) was added dropwise over 10 minutes. The mixture was stirred for 0.5 hour, allowed to warm to -20°C and formaldehyde gas bubbled through the mixture until no starting material remained, as determined by glc analysis. On completion  
15 of the reaction, the mixture was treated with water, the ether phase separated, the aqueous phase extracted with ethyl acetate (twice) and the organic extracts combined and washed with water (three times). The combined organic extract was dried over magnesium sulphate and evaporated under reduced pressure to give the required product (24.96g) as a pale yellow liquid.
- 20 <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.00(12H, s); 0.46(4H, s); 1.32(6H, s); 4.10(2H, s).

The 1-(1,1-Dimethyl-2-propynyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane used above was prepared using a recipe similar to the following. 3-Amino-3-methylbutyne (commercially available as 90% aqueous solution; 16.6g) was dissolved in dichloromethane (150ml), dried over sodium sulphate and filtered to give a

solution containing 14.9g of amine. To the stirred solution of amine under an atmosphere of nitrogen at ambient temperature was added dry triethylamine (48.4ml). 1,2-Bis-(chlorodimethylsilyl)ethane (38.98g) in dichloromethane (100ml) was then added dropwise, maintaining the reaction temperature at 15°C by cooling. The mixture was stirred for 3 hours, the colourless solid, which had formed during the reaction, was filtered from solution and the filtrate was evaporated under reduced pressure to give a paste. The paste was extracted into hexane and refiltered. The filtrate was evaporated under reduced pressure and the oil obtained was distilled to give 1-(1,1-dimethyl-2-propynyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane, 21.5g, b.p. 41°C at 0.06 mm Hg pressure.

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.16(12H, s); 0.60(4H, s); 1.48(6H, s); 2.24(1H, s).

#### Step 2

The product from Stage 1, Step 1 (24.96g) was treated with dilute aqueous hydrochloric acid (300ml) and stirred at ambient temperature for 0.5 hour. The mixture was washed with diethyl ether (twice), the aqueous phase was evaporated under reduced pressure, distilled with toluene (twice) to remove residual water and the residual solid obtained was triturated with hexane to give 4-amino-1-hydroxy-4-methylpent-2-yne hydrochloride (13.1g) as a cream coloured solid.

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.48(6H, s); 4.06(2H, s); 5.32(1H, s); 8.64(3H, s).

#### Stage 2: Preparation of 4-amino-1-tert.-butyldimethylsilyloxy-4-methylpent-2-yne

4-Amino-1-hydroxy-4-methylpent-2-yne hydrochloride (4.40g) was dissolved in dry *N,N*-dimethylformamide (100ml) and triethylamine (4.44ml) was added. The suspension was stirred at ambient temperature for 10 minutes then imidazole (4.93g) was added followed by *tert*-butyldimethylsilyl chloride (5.24g) in dry *N,N*-dimethylformamide (40ml). The mixture was stirred at ambient temperature for 18 hours and diluted with water. The aqueous mixture was extracted with diethyl ether (three times), the organic extracts combined, washed with water (twice), dried over magnesium sulphate and evaporated under reduced pressure to give the required product (6.88g) as a yellow liquid.

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.04(6H, s); 0.84(9H, s); 1.30(6H, s); 4.22(2H, s).

#### Stage 3

2-(3,5-dichlorophenoxy)-butyric acid (prepared as described in US 4116677; 2.61g), 4-amino-1-tert.-butyldimethylsilyloxy-4-methylpent-2-yne (2.27g) and 4-dimethylaminopyridine (0.010g) in dry dichloromethane (50ml) were stirred together and

*N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride ( 2.11g) was added. The mixture was stirred at ambient temperature for 2.5 hours, stored for 18 hours, diluted with dichloromethane, washed with saturated aqueous sodium hydrogen carbonate (twice) then with water (twice). The organic phase was dried over magnesium sulphate and evaporated under reduced pressure to give a yellow oil. The oil was fractionated by chromatography (silica; hexane/ethyl acetate, 1:1 by volume) to give the required product (3.50g) as a colourless oil.

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.10(6H, s); 0.90(9H, s); 0.98-1.02(3H, t); 1.62-1.64(6H, d); 1.90-1.98(2H, m); 4.32(2H, s); 4.36-4.40(1H, t); 6.30(1H, s); 6.82(2H, s); 7.02(1H, s).

## EXAMPLE 2

This Example illustrates the preparation of 2-(3,5-dichlorophenoxy)-*N*-(1-hydroxymethyl-4-methylpent-2-yn-4-yl) butyramide (Compound No. 4 in Table1)

2-(3,5-Dichlorophenoxy)-*N*-(1-*tert*-butyldimethylsilyloxy-4-methylpent-2-yn-4-yl)butyramide (prepared as described in Example 1; 3.35g) in tetrahydrofuran (60ml) was stirred at 3-5°C and a solution of *tetra n*-butylammonium fluoride (14.6ml of 1M solution in tetrahydrofuran) was added dropwise over 5 minutes. On completion of the addition, the mixture was stirred for 0.5 hour at 0°C, 2 hours at ambient temperature and stored for 18 hours. The solvent was evaporated under reduced pressure and the residue partitioned between ethyl acetate and aqueous ammonium chloride. The organic phase was separated, washed with aqueous ammonium chloride, brine, dried over magnesium sulphate and evaporated under reduced pressure to give a colourless solid that was fractionated by chromatography (silica; hexane/ethyl acetate, 2:1 by volume) to give the required product as a colourless solid (2.01g) mp 104-106°C.

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.00-1.04(3H, t); 1.60-1.62(6H, d); 1.92-2.00(2H, m); 2.02-2.06(1H, t); 4.28-4.30(2H, d); 4.38-4.42(1H, t); 6.30(1H, s); 6.86(2H, s); 7.04(1H, s).

## EXAMPLE 3

This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(1-methoxy-4-methylpent-2-yn-4-yl) butyramide (Compound No. 4 in Table 11)

2-(3,5-Dichlorophenoxy)-*N*-(1-hydroxymethyl-4-methylpent-2-yn-4-yl)butyramide (prepared as described in Example 2; 1.54g) in dry *N,N*-dimethylformamide (20ml) was added dropwise over 5 minutes to a suspension of sodium hydride (0.28g, 80% dispersion in mineral oil) in dry *N,N*-dimethylformamide (2ml) under an atmosphere

of nitrogen at ambient temperature. The mixture was stirred for 2 hours and methyl iodide (0.71g) in dry *N,N*-dimethylformamide (5ml) was added over 1 minute at ambient temperature. The mixture was stirred for 2 hours and stored at ambient temperature for 18 hours. Water was added and the mixture extracted with ethyl acetate (three times). The  
5 extracts were combined, washed with water (twice), dried over magnesium sulphate and evaporated under reduced pressure to give a gum that was fractionated by chromatography (silica; hexane/ethyl acetate, 4:1 by volume) to give the required product (0.44g) as a colourless solid, mp 103-104°C.

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.98-1.04(3H, t); 1.64(6H, s); 1.92-2.00(2H, q); 3.36(3H, s);  
10 4.12(2H, s); 4.38-4.42(1H, t); 6.30(1H, s); 6.84(2H, s); 7.04(1H, s).

#### EXAMPLE 4

This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(1-chloro-6-methylhept-4-yn-6-yl) butyramide (Compound No. 4 in Table 52)

##### Stage 1: Preparation of 1-chloro-6-methylhept-4-yn-6-ylamine hydrochloride

##### Step 1: Preparation of 6-(1-chloro-6-methylhept-4-yn-6-yl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane

*n*-Butyl lithium (97.6ml, 2.5M in hexanes) was added dropwise over 0.5 hours to a stirred solution of 1-(1,1-dimethyl-2-propynyl)-2,2,5,5-tetramethyl-1-aza-2,5-disilacyclopentane (55.1g) in dry tetrahydrofuran (450ml) under an atmosphere of nitrogen at  
20 -70°C. The mixture was stirred for 1.5 hours at -70°C, allowed to warm to -15°C then a solution of 1-chloro-3-iodopropane (55.0g) in dry tetrahydrofuran (50ml) was added dropwise over 20 minutes whilst allowing the reaction temperature to slowly warm to 0°C. On complete addition, the reaction mixture was stirred at ambient temperature for 4.25 hours then stored for 18 hours. The mixture was diluted with water and extracted  
25 with ethyl acetate (twice). The extracts were combined, washed with water (three times), dried over magnesium sulphate then evaporated under reduced pressure to give the required product as an orange liquid, 78.5g, <sup>1</sup>H NMR (CDCl<sub>3</sub>) 0.00(12H, s); 0.46(4H, s); 1.30(6H, s); 1.76(2H, m); 2.18(2H, t); 2.46(2H, t).

##### Step 2: Preparation of 1-chloro-6-methylhept-4-yn-6-ylamine hydrochloride

30 The product from Step 1 (78.5g) was stirred at -5°C and dilute aqueous hydrochloric acid (785ml, 2M) was slowly added, maintaining the reaction temperature below 30°C during the addition. On complete addition, the mixture was stirred for a further 1 hour at ambient temperature, washed with diethyl ether (twice), evaporated

under reduced pressure and the residual water removed by azeotropic distillation with toluene. The solid obtained was dissolved in dichloromethane, dried over magnesium sulphate and evaporated under reduced pressure to give the required product as a cream coloured solid, 36.5g, <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.74(6H, s); 1.97(2H, m); 2.39(2H, m); 3.68(2H, t); 8.80(3H, broad s).

Stage 2: Preparation of 2-(3,5-dichlorophenoxy)-N-(1-chloro-6-methylhept-4-yn-6-yl) butyramide

1-Chloro-6-methylhept-4-yn-6-ylamine hydrochloride (9.8g) in *N,N*-dimethylformamide (250ml) containing triethylamine (10.4ml) was stirred at ambient temperature for 10 minutes. The suspension which had formed was treated sequentially with 1-hydroxybenzotriazole (7.59g), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (10.56g) then 2-(3,5-dichlorophenoxy)-butyric acid (13.07g) in *N,N*-dimethylformamide (50ml). The mixture was stirred at ambient temperature for 2 hours, stored for 18 hours then poured into water. The product was extracted with ethyl acetate (three times). The extracts were combined, washed with a saturated aqueous solution of sodium hydrogen carbonate and water (three times) and dried over magnesium sulphate. They were then evaporated under reduced pressure to give the required product as a yellow gum (19.1g) sufficiently pure for further derivatisation. A portion of the gum (0.33g) was fractionated by chromatography (silica; hexane/ diethyl ether, 4:1 by volume) to provide a pure sample of 2-(3,5-dichlorophenoxy)-*N*-(1-chloro-6-methylhept-4-yn-6-yl) butyramide as a colourless oil, 0.22g, <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.00-1.04(3H, t); 1.58(6H, s); 1.90-2.00(4H, m); 2.36-2.40(2H, t); 3.62-3.66(2H, t); 4.36-4.40(1H, t); 6.26(1H, s); 6.84(2H, s); 7.02(1H, s).

EXAMPLE 5

This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(6-methyl-1-methylthio-hept-4-yn-6-yl) butyramide (Compound No. 4 in Table 53)

2-(3,5-Dichlorophenoxy)-*N*-(1-chloro-6-methylhept-4-yn-6-yl) butyramide (0.78g) in dry *N,N*-dimethylformamide (10ml) containing sodium methylthiolate (0.15g) was stirred at ambient temperature under an atmosphere of nitrogen for 2 hours then stored for 2 days. The reaction mixture was diluted with water, extracted with ethyl acetate (three times) and the extracts were combined, washed with water (three times), dried over magnesium sulphate then evaporated under reduced pressure to give a gum. The gum was fractionated by chromatography (silica; hexane/ diethyl ether 2:1 by

volume) to give the required product as a colourless oil, 0.53g,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 0.98-1.02(3H, t); 1.60(6H, s); 1.74-1.82(2H, m); 1.92-2.00(2H, m); 2.10(3H, s); 2.28-2.34((2H, t); 2.56-2.60(2H, t); 4.36-4.40(1H, t); 6.26(1H, s); 6.84(2H, s); 7.04(1H, s).

#### EXAMPLE 6

This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(6-methyl-1-methylsulphinyl-hept-4-yn-6-yl) butyramide (Compound No. 4 in Table 54)

To a stirred solution of 2-(3,5-dichlorophenoxy)-*N*-(6-methyl-1-methylthio-hept-4-yn-6-yl) butyramide (0.21g) in ethanol (2.5ml) at ambient temperature was added dropwise a solution of sodium periodate (0.13g) in water (2.5ml). The mixture was stirred for 2.5 hours, stored for 18 hours then evaporated under reduced pressure. The residue was extracted with dichloromethane and the organic phase filtered then evaporated under reduced pressure to give the required product as a colourless oil, 0.18g,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 0.98-1.02(3H, t); 1.56(3H, s); 1.58(3H, s); 1.92-2.00(4H, m); 2.34-2.42((2H, m); 2.62(3H, s); 2.76-2.84(1H, m); 2.90-2.96(1H, m); 4.34-4.38(1H, m); 6.26(1H, s); 6.82(2H, s); 7.02(1H, s).

#### EXAMPLE 7

This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(6-methyl-1-methylsulfonyl-hept-4-yn-6-yl) butyramide (Compound No. 4 in Table 55)

To a stirred solution of 2-(3,5-dichlorophenoxy)-*N*-(6-methyl-1-methylsulphinyl-hept-4-yn-6-yl) butyramide (0.10g) in dichloromethane (5ml) at  $0^\circ\text{C}$  was added 3-chloroperbenzoic acid (0.060g, 70%, stabilised with water). The mixture was stirred for 0.5 hours at  $0^\circ\text{C}$ , then for 1 hour at ambient temperature and stored for 18 hours. The solvent was evaporated under reduced pressure and the residue dissolved in diethyl ether, washed with a saturated aqueous solution of sodium hydrogen carbonate (three times) and water (twice), dried over magnesium sulphate and then evaporated under reduced pressure to give a colourless oil. The oil was fractionated by chromatography (silica; hexane /ethyl acetate, 2:1 by volume) to give the required product as a pale yellow oil, 0.040g,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 0.98-1.02(3H, t); 1.56(3H, s); 1.58(3H, s); 1.92-2.00(4H, m); 2.36-2.40((2H, t); 2.96(3H, s); 3.22-3.26(2H, m); 4.38-4.42(1H, t); 6.26(1H, s); 6.84(2H, s); 7.02(1H, s).

## EXAMPLE 8

This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(1-methoxy-6-methylhept-4-yn-6-yl) butyramide (Compound No. 4 in Table 57)

To a stirred solution of sodium methoxide (prepared from sodium, 0.014g) in  
5 methanol (2ml) at ambient temperature was added 2-(3,5-dichlorophenoxy)-*N*-(1-chloro-6-methylhept-4-yn-6-yl) butyramide (0.20g) followed by further sodium methoxide (0.3g) and sodium iodide (0.1g). The mixture was stirred at ambient temperature under an atmosphere of nitrogen for 4 hours, heated to reflux for a total of 10 hours, cooled to ambient temperature then stored for 18 hours. The reaction mixture was diluted with  
10 water, extracted with ethyl acetate (three times) and the extracts were combined, washed with brine then evaporated under reduced pressure to give a yellow oil. The oil was fractionated by chromatography (silica; hexane/ethyl acetate, 3:1 by volume) to give the required product as a colourless oil, 0.055g, <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.98-1.04(3H, t); 1.60(6H, s); 1.72-1.78(2H, m); 1.92-2.00(2H, m); 2.24-2.28(2H, t); 3.34(3H, s); 3.42-  
15 3.46(2H, t); 4.36-4.38(1H, t); 6.28(1H, s); 6.84(2H, s); 7.02(1H, s).

## EXAMPLE 9

This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(6-methyl-1-(1,2,4-triazol-1-yl)-hept-4-yn-6-yl) butyramide (Compound No. 4 in Table 56)

To a stirred solution of 2-(3,5-dichlorophenoxy)-*N*-(1-chloro-6-methylhept-4-yn-6-yl) butyramide (0.59g) in dry *N,N*-dimethylformamide (10ml) containing anhydrous  
20 potassium carbonate (0.28g) was added 1,2,4-triazole (0.10g). The mixture was heated to 90°C for 2.75 hours, cooled to ambient temperature, diluted with water and extracted with ethyl acetate (three times). The extracts were combined, washed with brine, dried over magnesium sulphate then evaporated under reduced pressure to give a yellow oil.  
25 The oil was fractionated by chromatography (silica; hexane /ethyl acetate, 2:1 by volume followed by ethyl acetate) to give the required product as a colourless oil, 0.16g, <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.00-1.06(3H, t); 1.60(3H, s); 1.62(3H, s); 1.92-2.14(6H, m); 4.38-4.44(3H, m); 6.26(1H, s); 6.84(2H, s); 7.04(1H, s); 7.96(1H, s); 8.32(1H, s).

## EXAMPLE 10

30 This Example describes the preparation of 2-(3,5-dichlorophenoxy)-*N*-(1-cyano-6-methylhept-4-yn-6-yl) butyramide (Compound No. 4 in Table 41)

A stirred solution of 2-(3,5-dichlorophenoxy)-*N*-(1-chloro-6-methylhept-4-yn-6-yl) butyramide (3.91) in dry *N,N*-dimethylformamide (35ml) containing potassium



cyanide (0.78g) was heated to 95°C for 6 hours, cooled to ambient temperature then stored for 18 hours. The mixture was poured into water, extracted with diethyl ether (three times) and the extracts were combined, washed with water (three times), dried over magnesium sulphate then evaporated under reduced pressure to give the required product as a yellow oil, 3.42g. A portion of this material was fractionated by chromatography (silica; hexane/ethyl acetate 3:1 by volume) to give a pure sample of 2-(3,5-dichlorophenoxy)-*N*-(1-cyano-6-methylhept-4-yn-6-yl) butyramide as a yellow gum, <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 0.98-1.02(3H, t); 1.58(3H, s); 1.60(3H, s); 1.82-1.88(2H, m); 1.92-1.98(2H, m); 2.36-2.40(2H, t); 2.48-2.56(2H, m); 4.38-4.42(1H, t); 6.26(1H, s); 6.84(2H, s); 7.04(1H, s).

#### EXAMPLE 11

This Example illustrates the fungicidal properties of compounds of formula (1).

The compounds were tested in a leaf disk assay, with methods described below. The test compounds were dissolved in DMSO and diluted into water to 200 ppm. In the case of the test on *Pythium ultimum*, they were dissolved in DMSO and diluted into water to 20 ppm.

*Erysiphe graminis f.sp. hordei* (barley powdery mildew): Barley leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

*Erysiphe graminis f.sp. tritici* (wheat powdery mildew): Wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

*Puccinia recondita f.sp. tritici* (wheat brown rust): Wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed nine days after inoculation as preventive fungicidal activity.

*Septoria nodorum* (wheat glume blotch): Wheat leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry

completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

5 *Pyrenophora teres* (barley net blotch): Barley leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

10 *Pyricularia oryzae* (rice blast): Rice leaf segments were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

15 *Botrytis cinerea* (grey mould): Bean leaf disks were placed on agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

20 *Phytophthora infestans* (late blight of potato on tomato): Tomato leaf disks were placed on water agar in a 24-well plate and sprayed with a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed four days after inoculation as preventive fungicidal activity.

25 *Plasmopara viticola* (downy mildew of grapevine): Grapevine leaf disks were placed on agar in a 24-well plate and sprayed a solution of the test compound. After allowing to dry completely, for between 12 and 24 hours, the leaf disks were inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed seven days after inoculation as preventive fungicidal activity.

30 *Pythium ultimum* (Damping off): Mycelial fragments of the fungus, prepared from a fresh liquid culture, were mixed into potato dextrose broth. A solution of the test compound in dimethyl sulfoxide was diluted with water to 20ppm then placed into a 96-well microtiter plate and the nutrient broth containing the fungal spores was added. The test plate was incubated at 24°C and the inhibition of growth was determined photometrically

after 48 hours.

The following Compounds [Compound No (Table)] gave more than 60% control of the following fungal infections at 200ppm:

*Phytophthora infestans*: 4(1), 4(11), 4(41), 4(51), 4(53), 4(54), 4(55), 4(56), 4(57).

5 *Plasmopara viticola*: 4(1), 4(11), 4(41), 4(51), 4(52), 4(53), 4(54), 4(55), 4(56), 4(57)

*Pyrenophora teres*: 4(57).

*Erysiphe graminis f.sp. hordei*: 4(1), 4(11), 4(21).

*Erysiphe graminis f.sp. tritici*: 4(11), 4(41), 4(57).

The following Compounds gave more than 60% control of the following fungal infection

10 at 20ppm:

*Pythium ultimum*: 4(1), 4(11), 4(53), 4(54), 4(57).